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THE AMERICAN
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VOL. 100 JULY, 1928 NO. 7

EDITORIAL

WITH THE PASSING away of George M. Beringer, who died at his home in Collingswood, New Jersey, June 23d, Pharmacy lost one of its ablest practitioners. Hardly a niche in the pharmaceutical structure that this man had not, at some time or another, capably filled. In retail pharmacy, the store which he conducted was known throughout his city and State as a place where reliable medicines could be purchased—and it was his personality that filled the establishment and made its name and its proprietor's name synonymous with ethical service. Manufacturing pharmacy was another field where his efforts were most fruitful. The company, which his initiative recently organized, was already well established and here, too, it was his active direction of affairs that insured success.

Pharmaceutical education had long been favored with his good offices. While chairman of the Board of Trustees of the Philadelphia College of Pharmacy and Science he had done much to advance the status of pharmaceutical training and to improve its curriculum.

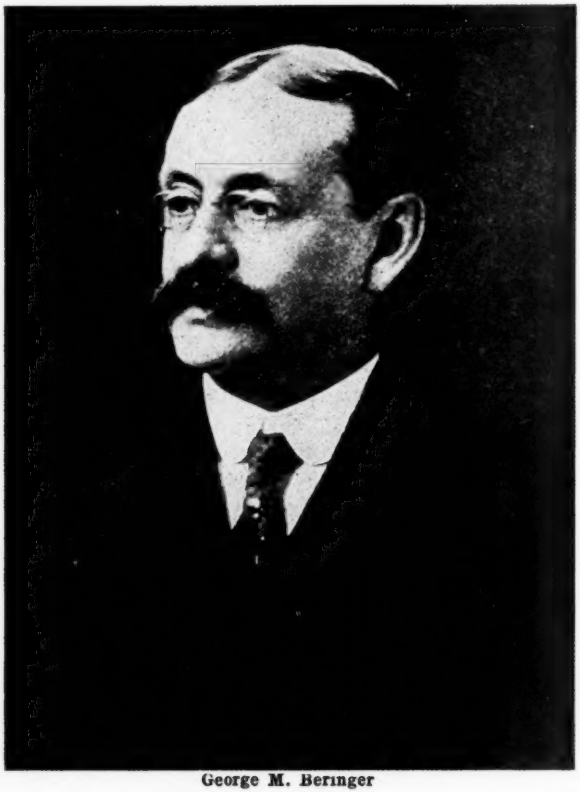
As a writer on topics chemical and pharmaceutical he wielded a lucid, facile pen and the period of his editorship of the *American Journal of Pharmacy* during the trying days of the great World War found him extremely active in this direction. His editorials were couched in fearless, virile language—for he never hesitated to wordhandle a cause which he considered important enough to be admitted to the pages of his journal.

In Pharmacopœial and National Formulary revision his services were such that it were not uncomplimentary to anyone for us to state that his place will be extremely difficult to fill from the ranks of retail pharmacists.

In revision work he was not only a meticulous proofreader, but far beyond that in service, he was a meticulous experimenter. And his experiments were innumerable and invaluable.

To the end of his earthly days he was earnestly working in the pharmacopœial field.

The chairman of the Revision Committee has written that:



George M. Beringer

"His interest and help in pharmacopœial revision did not cease when the revision ended, for he was at this time directing several of the researches now under way in the Committee of Revision, with a conference on the subject, arranged for this week."

In association work, too, his energies had been untiring and the American Pharmaceutical Association honored him with the presidency in 1913.

Indeed, he was the rare type of worker who could turn his hand to any part of his chosen life work and by diligence and good sense bring it to a successful end.

Pharmacy, of the generation just passing, has been well blessed with men of work and worth, and Beringer was one of these splendid exemplars of what was best in the pharmacy of the day just closing.

Professor E. Fullerton Cook, chairman of the Pharmacopœial Revision Committee, in announcing the death of his colleague, writes that:

> "Mr. Beringer unsparingly has expended of his time and energy in every field of professional pharmacy during a full generation, and the stamp of his personality and high ideals is reflected throughout this entire period in the A. Ph. A., the U. S. Pharmacopœia, his Alma Mater, and in pharmaceutical literature."

Surely this is a tribute to versatility and to diligence. So that the journal which he so long and so ably edited may carry the record, a brief résumé of his career is herewith appended:

> "George Mahlon Beringer, son of Levi D. and Rebecca Beringer, was born in Philadelphia on February 3, 1860. He obtained his early education in the public schools, graduating from the Central High School in 1876, with the degree of A. B. He immediately entered the employ of Bullock and Crenshaw, and graduated from the College in 1880, the subject of his thesis being 'Caffeina.' Subsequently, he engaged in laboratory work with Bullock and Crenshaw, and later became a department manager.
>
> "In 1892 he was chosen Director of the Microscopical Laboratory conducted by the Alumni Association of the Philadelphia College of Pharmacy and performed the duties of this position until the Association turned the laboratory over to the College in 1894.
>
> "Mr. Beringer remained with Bullock and Crenshaw until June 1, 1892, when he purchased from the estate of Albert P. Brown, the latter's store at Fifth and Federal Streets, Camden, N. J., and continued the business, in the conduct of which he has been eminently successful.
>
> "He is a life member of the Philadelphia College of Pharmacy, and was elected a trustee in 1893. He was active in the affairs of the College for many years, especially as a member of the committee on publication and the committee on instruction of the Board of Trustees, rendering valuable service. He was given

the honorary degree of master in pharmacy by the College in 1903. He was elected chairman of the Board of Trustees in 1910. In 1917 he became editor of the *American Journal of Pharmacy* and did much to develop that periodical during his four years of service as editor.

"Mr. Beringer was a member of the Committee of Revision of the U. S. Pharmacopœia of 1910, and the Committee on National Formulary of the American Pharmaceutical Association of 1908, in the work of which his comprehensive knowledge of pharmacy and allied sciences and his critical judgment did much to give to the U. S. Pharmacopœia (IX) and the National Formulary (IV) their practicality. He is a member of the present Committee of Revision of the U. S. Pharmacopœia and the Committee on National Formulary.

"He has taken deep interest in the work of the American Pharmaceutical Association, having been elected a member in 1893; chairman of the section on practical pharmacy and dispensing in 1902-1903; and president of the Association in 1913-1914.

In 1924 he was awarded the Remington Honor Medal in recognition of his high services to pharmacy.

Commenting upon this award, the *Public Ledger* of Philadelphia, in a leading article, wrote as follows:

"Hundreds daily pass little shops tucked in among more luxurious buildings and the thought must frequently occur to the passersby concerning what transpires behind those mysterious doors. It is in places of this kind, however, that history is made, strides in medicine take place and science is advanced.

"Little do the hundreds who daily pass the unpretentious building at Fifth and Federal Streets, Camden, realize that it is there that conspicuous service along pharmaceutical lines had been rendered and for which the Remington Honor Medal, the highest distinction in American pharmacy, was recently bestowed.

"This medal is awarded each year to that member of the pharmaceutical profession who, in the opinion of a committee of judges, has advanced it in scientific work, or in educational or industrial field. It was established six years ago by the New York Branch of the American Pharmaceutical Association in honor of the late Dr. Joseph P. Remington, who for many years was dean of the Philadelphia College of Pharmacy and a leader in pharmaceutical work in America. The jury of award consists of the ex-presidents of the National Association.

"At the annual meeting of this committee, held last week in Newark, the name of Dr. George M. Beringer, of Camden, was submitted, and finally decided upon for this signal honor. The

award was not made, however, for any one conspicuous piece of work on the part of Dr. Beringer, but for a culmination of activities covering a long period of years, and included work along educational, association and industrial lines."

There is left to mourn his loss, his widow, his son, George—an able pharmacist, under whose direction the business enterprises are to be continued—and all who knew him and appreciated his worth and his services to his beloved calling. God bless his memory—and prosper his ideals.

IVOR GRIFFITH.

SELECTED EDITORIAL

FRIEDRICH WÖHLER AND UREA, 1928*

THE PRESENT YEAR marks the hundredth anniversary of Friedrich Wöhler's publication of the discovery of the synthesis of urea. This discovery, the outcome of a series of investigations of cyanic acid and its compounds, represents the first production in the laboratory of an organic substance without the intervention of living matter. In his article of four small pages, detailing what has been called one of the most important contributions to chemistry, Wöhler said: "I obtained the unexpected result that, when cyanic acid and ammonia are combined, urea is produced. This fact is all the more remarkable because it offers an example of the artificial formation of an organic compound, moreover of an animal substance, by means of inorganic materials." The synthesis of urea was the first experimental evidence to disprove the doctrine of "vital force" as the cause of chemical transformations within living organisms—chemical reactions which, from points conceded, could not be duplicated in the laboratory. Concerning this epoch-making discovery, Professor Hofmann wrote in his biography of Wöhler: "The present generation, which is constantly gathering such rich harvests from the territory won for it by Wöhler, can only with difficulty transport itself back to that remōte period in which the creation of an organic compound within the body of an animal or plant appeared to be conditioned in some mysterious way by the vital force, and they can hardly realize

*Reprinted from *Journal of the American Medical Association.*

the impression which the building up of urea from its elements made on men's minds." Further progress in synthetic chemistry, however, was not rapid in the beginning. Nearly twenty years elapsed before another example of the synthesis of an organic compound from inorganic sources was worked out, this being acetic acid, in 1845 by Kolbe, one of Wöhler's most illustrious pupils.

Wöhler's reputation rests on many distinguished and fundamental contributions to chemistry. Throughout a long lifetime, unusually fruitful for the sciences on which medicine rests, he published more than 250 original papers. Educated in medicine at Marburg and at Heidelberg, after graduating from the latter institution in 1823 he followed the advice of his teacher Leopold Gmelin, and devoted his life to chemistry. In 1827, at the age of 27, he isolated for the first time aluminum and beryllium, and the rare earth element yttrium, by fusion of the salts of these metals with potassium. In collaboration with Liebig he investigated the oil of bitter almonds and in this classic research laid the foundation for the present theory of organic radicals. With Liebig also he studied the chemistry of uric acid and prepared a considerable number of the derivatives of this substance. Although many of Wöhler's later investigations dealt with inorganic or mineral chemistry, his discovery that benzoic acid taken in with the food appears as hippuric acid in the urine may be considered one of the starting points of the modern chemistry of metabolism. In 1860 he prepared cocaine in pure crystalline form from coca leaves, and his published account of the properties of cocaine mentioned that it had a bitter taste and temporarily rendered insensitive the parts of the tongue with which it came in contact. The practical use of cocaine as an anesthetic was not developed until 1884, when it was introduced by the ophthalmologist Koller. Not the least of Wöhler's activities was his teaching. He made the University of Göttingen famous as a school of chemistry, and before his death in 1882 thousands of students had received their training in his laboratory. Among his most influential pupils were Fittig, Kolbe and Beilstein, and the Americans Ira Remsen and Edgar Fahs Smith.

Of all Wöhler's achievements during his lifetime of devotion to science, the synthesis of urea is probably the most noteworthy. The American Chemical Society plans to celebrate the centenary of this achievement by a special program at its Boston meeting in September. With the publication of Wöhler's classic paper, synthetic chemistry may be said to have had its origin. All the accomplishments of this

science—the synthesis of dyes identical with natural coloring matters, and innumerable others that have no counterpart in the animal or vegetable world; the artificial formation of sugars and polypeptides and fats; the artificial preparation of drugs, of epinephrine, of thyroxin, and of many others so well known as to be accepted commonplaces of the present day—are among the "rich harvests" of Wöhler's fundamental contribution.

ORIGINAL ARTICLES

STUDIES IN THE GENUS MENTHA*

16. THE NON-VOLATILE CONSTITUENTS OF MENTHA AQUATICA, LINNE

By Samuel M. Gordon†

MENTHA PIPERITA L., on the basis of systematic botany, is considered to be a hybrid resulting from Mentha aquatica L. on the one hand and Mentha viridis L. on the other.[1] Unfortunately, the hybridization has not yet been accomplished experimentally. The fusion plant yields menthol as the principal component of its volatile product, whereas the parent plants yield linalool and carvone, respectively, as the main constituent of their volatile oils. If the theoretical morphological deductions as to the hybrid nature of *M. piperita* are correct, it is thus apparent that wide but definite differences exist in the anabolism of components of the oil within three closely related species. If the production of oil results from a definable process then the changes brought about in the oils by hybridization might lead to a clearer conception of hereditary processes.[2] The results upon which this thesis rests have been made in earlier papers of this series; and the hypothetical grounds of the course followed in the elaboration of the oil has been separately reported.[3]

*From the Laboratory of Phytochemistry, University of Wisconsin.

†National Research Fellow in the Biological Sciences.

[1] On the authority of Briquet, cp. Tschirch, A., *Hand. d. Pharmakognosie.*

[2] Bacon, F. J., Jenison, G. C., and Kremers, R. E., *J. Am. Pharm. Assoc.*, 1923, XII, 1075.

[3] Kremers, R. E., *J. Biol. Chem.*, 1922, L. 31.

While the chemistry of the volatile products has been worked out in some detail with the above theses in view, *nothing whatever* is known of the non-volatile constituents of any of these three plants. The investigation herewith reported on the non-volatile constituents of M. aquatica L. was undertaken in order to throw some light on the differences in constitution of the non-volatile constituents, other than proteins, in these three closely related plants. Mentha piperita is now being investigated in this laboratory, and it is hoped to extend the investigation to the third plant of the group, namely, M. viridis in the near future. While it is yet too early to point out differences in composition of the two plants now under investigation, preliminary results show differences in the products found in the non-saponifiable portion. A more complete discussion of the differences, however, must be left until that part of the investigation is complete. In the present report, only the results of the isolation of the constituents from M. aquatica will be detailed.

In passing, the need for more desirable methods for the study of leaf fats should be mentioned. In a review published several years ago, E. Frankland Armstrong stated: ". . . it is almost without exception in the fruits and seeds that the mixtures of glycerides which constitute the vegetable fats are found."[4] While exceptions may well be taken to the statement, it nevertheless reflects the lack of knowledge regarding the chemistry of the leaf fats.

In this investigation the leaves showed a content of about 7 per cent. fatty material. Whereas the one-half per cent. of volatile constituents has been examined with some care, the 7 per cent. of fatty oil have not even been mentioned heretofore. The difficulty lies in obtaining the free fatty acids in sufficiently pure form for analysis and determination of the constants. The difficulty is principally due to the presence of the green coloring matter, which is very difficult to remove on account of its high solubility in the fat and the usual fat solvents. It obviously would have been desirable to remove the coloring matter by mild treatment before proceeding with a close examination, but this was a hopeless task. Hence esterification and subsequent distillation under reduced pressure was resorted to. While this procedure yielded almost colorless products, much loss took place.

The examination of the non-saponifiable portion yielded inter-

[4] Armstrong, E. F., and Allan, J., *J. Soc. Chem. Ind.*, 1924T, XLIII, 207.

esting results. In addition to a pigment, presumably of a carotinoid nature, there were found linalool, dotriacontane, lupeol, α-sitosterol and an oil. The oil boiled over a wide range, 105-225 degrees C. at 15 mm., and gave very intense color reactions with Liebermann-Burchard, Hager-Salkowski and Whitby reagents for sterols. It is not precipitated by digitonin; it is unsaturated since it yields high iodine values.

The liquid products may prove of interest as a possible "vitamine precursor" because of its apparent similarity to the oil from the non-saponifiable fraction of wheat-germ oil found by Evans and Burr to be active as an anti-sterility factor.[5] This portion of the work is now being repeated on a larger amount of starting material in order to study the oil in greater detail and to test its biological properties.

Experimental

The material used in this investigation was kindly supplied by the Office of Drug and Poisonous Plant Investigations, Dr. W. W. Stockberger in charge, Bureau of Plant Industry, Department of Agriculture. It had been cured from plants raised in the Experimental Gardens at Washington, D. C. The writer not only desires to make due acknowledgment but also to thank all who were so kind as to co-operate.

Test for hydrocyanic acid. 100 gms. of the ground material were covered with 400 cc. of distilled water. After standing over night, the liquid was steam distilled. The distillate yielded a negative test with silver nitrate and with potassium hydroxide, ferrous sulphate and ferric chloride. The absence of hydrogen cyanide is thus shown.

Pentosan determination. The determination was made according to the Official Methods of the Association of Agricultural Chemists and showed 3.65 per cent. of furfural, corresponding to 7.05 per cent. pentose and 6.22 per cent. pentosan. As will be seen further on, the volatile oil obtained gave a slightly positive test for furfural. The small amount in the volatile oil, however, indicates that the furfural may have been derived by decomposition of pentosan material.

[5] Evans, H. M., and Burr, G. O., *Proc. Natl. Acad. Sci.*, 1925, XI, 334.

Extraction of the Plant with Alcohol

For the purposes of a complete examination the main portion of the dried, ground leaves, amounting to 13.78 kilos, was thoroughly extracted by percolation with 95 per cent. alcohol in the Lloyd extractor of the Wisconsin Pharmaceutical Experiment Station. The percolate was drawn off from time to time (to avoid continued heating of the extract); the residual alcohol recovered by distillation from a water bath and returned to the extractor. The last batch of alcohol recovered was removed for further examination as subsequently described.

The final extract, which measured about twelve liters, was a very dark viscous liquid showing the characteristic light reactions of chlorophyll to reflected light. This liquid was acid to litmus; and was distilled from a steam bath in order to remove alcohol as completely as possible. The pitch black extract weighed, after drying, 2.6 kilos or 18.8 per cent. of the plant material used.

In the course of the extraction a very small amount of almost white crystals separated in the levelling tube of the apparatus. These were recovered, washed with alcohol and dried. Qualitative tests showed these to be potassium nitrate, a large amount of which was separated from the aqueous extract.

Distillation of the Alcoholic Extract With Steam and Separation of the Essential Oil

After having removed the alcohol as completely as possible, the dark colored residual extract was distilled in a current of steam and the distillate collected through a Florentine flask. A little alcohol passed over at first and subsequently the liquid became milky with the separation of volatile oil. The volatile oil was separated from the aqueous liquid and amounted to 108 gms. This, together with the 8.6 gms. recovered from the aqueous-alcoholic solution, amounted to 0.846 per cent. of the leaves. Attempts to cohobate the aqueous portions of the steam distillate were unsuccessful, on account of the large amounts of alcohol, which evidently had been retained in the original extract. Hence, the distillate, after removal of the essential oil, was saturated with salt and extracted with small successive portions of heptane. The oil, after recovery of the heptane, weighed 8.6 gms. as already mentioned. The aqueous liquid was reserved for examination as described below.

Characteristics of the Essential Oil

The oil obtained by steam distillation was of a light yellow color, clear and with an odor reminding of linalool. A drop of the essential oil in about 5 cc. of glacial acetic acid gave on the addition of a drop of conc. sulphuric acid, a reddish violet color, which is characteristic for certain sesquiterpenes.[6] When treated with aniline acetate it gave a positive test for furfural. Phenols and ketones were presumably absent, as shown by volumetric tests with 5 per cent. sodium hydroxide and 30 per cent. sodium acid sulphite respectively.

Density $(\frac{21°}{21°})$	0.8649
$n_D^{25°}$ (Abbé)	1.4588
$[a]_D^{25°}$	2.54
Acid number	nil
Ester number	39.79
Ester number, after acetylization	120.5
Ester, per cent. as linalyl acetate	13.93
Alcohol, per cent. as linalool	36.43
Total alcohol	47.38
Free alcohol	36.43

The examination of the essential oil will be described in a subsequent communication.

Examination of the Aqueous Liquid From the Steam Distillation

The eight liters of aqueous liquid, from the steam distillation after removal of the essential oil reacted decidedly acid to litmus. Hence the liquid was neutralized with an excess of barium carbonate and the mixture filtered. The filtrate was distilled and the first portions collected in one liter of 3 per cent. hydrochloric acid for subsequent recovery of any bases present. The remainder of the solution was reduced to a small volume and allowed to further evaporate in a desiccator over solid potassium hydroxide. This yielded 32.0 gms. of a pure white salt, which was crystallized once from water.

[6] Power, F. B., and Chestnut, V. K., *J. Am. Chem. Soc.*, 1925, XLVII, 1763.

1. 0.6278 gms. subs. lost at 110° 0.0431 gms.
2. 0.7081 " " " " " 0.0482 "

Calc. for $(CH_3COO)_2Ba.H_2O$ Found
6.59 per cent. H_2O 1. 6.86 2. 6.81.

1. 0.5849 gms. anhydrous substance gave 0.5203 gms. $BaSO_4$.
2. 0.6599 " " " " 0.5874 " "

Calc. for $(CH_3COO)_2Ba$ Found
52.38 per cent. Ba 1. 52.38 2. 52.38.

From the barium salt, a silver salt was prepared and analyzed after drying at 110 degrees C.:

1. 0.0851 gms. subs. gave 0.0563 gms. Ag.
2. 0.1202 " " " 0.0776 " "

Calc. for CH_3COO Ag Found
64.6 per cent. Ag 1. 64.9 2. 64.6.

The acetic acid presumably has resulted from hydrolysis of linalyl acetate of the volatile oil.

Isolation of Trimethylamine. The acid liquor, which received the first runnings of the distillate from the barium carbonate treatment, was evaporated to dryness, dissolved in a small quantity of water, filtered and treated with chloroplatinic acid solution. The crystalline precipitate was collected, washed and analyzed after drying at 110 degrees.

0.0867 gms. subs. yielded 0.0321 gms. Pt.

Calc. for $[(CH_3)_3N]_2.H_2PtCl_6$ Found
36.96 per cent. Pt. 37.09

After the above-described operation of distillation with steam there remained in the distillation flask a dark reddish-brown aqueous liquid (A) together with a quantity of a black oily resinous material (B). When cold the aqueous portion was decanted and the resin washed with three successive portions of hot water, these washings being added to the main portion of the aqueous liquid.

Examination of the Aqueous Liquid (A)

The above-mentioned aqueous liquid was filtered. It amounted to about four liters and was concentrated under reduced pressure. The distillate was found to contain appreciable amounts of formic

acid. During the distillation, a quantity of a white crystalline body separated but was only removed when the solution had become too concentrated. In this way 58 gms. of an inorganic salt was obtained, which was shown to be potassium nitrate by the usual tests. The absence of chlorine and sodium was indicated by appropriate tests. The concentrated aqueous solution, which now measured 600 cc. was allowed to cool and extracted five times with 30 cc. portions of ether. The aqueous solution gave a dark green coloration with ferric chloride, but they appeared to contain no tannin.

The ethereal solution, which was yellowish brown, was dried over anhydrous sodium sulphate. After filtering, the greater part of the solvent was removed by distillation; the last portions being allowed to evaporate spontaneously. In this way 7.5 gms. of a dark brown, thick syrup was obtained, which appeared to contain no crystalline material. Hence the extract was again brought into solution with ether and extracted successively with a saturated solution of ammonium carbonate, 10 per cent. sodium carbonate and 5 per cent. sodium hydroxide. All the alkaline liquids were subsequently acidified with dilute sulphuric acid; the first two acid solutions were extracted with ether, while the last yielded a yellow solution of apparent colloidal characteristics.

The ethereal residues of the ammonium and sodium carbonate extraction yielded syrups from which nothing definite could be separated. Hence they were bulked and subjected to steam distillation. The distillate reacted slightly acid to litmus and yielded a slight violet coloration with ferric chloride, thus indicating the presence of a phenolic body. However, subsequent extraction with ether failed to remove any appreciable amount of material.

The acidified portion of the sodium hydroxide extract yielded a small amount of a finely divided pigment, suspended in the acidulated medium, and had the properties of a hydrophyllic colloid. The particles could not be separated on a hardened filter paper; nor could they be separated by centrifuging or by the addition of various electrolytes. The solid was finally obtained in the following manner: The yellow pigment was again taken up in 10 per cent. sodium hydroxide, diluted with water. The alkaline solution was made barely acid to congo red paper and the liquid concentrated under pressure. When the volume of the liquid was brought down to about 50 cc. the solid readily separated and was filtered on a hardened filter paper. About 0.08 gms. of a light yellow substance was obtained.

The material was very soluble in most organic solvents, hence the above treatment was again repeated. This yielded, after drying on a porous plate, a bright yellow pigment melting at 250-253 degrees. The reactions of the substance indicate it as belonging to the group of flavone pigments. It was, however, definitely shown not to be quercitin by a negative test with Fehling's solution.

Treatment of the Aqueous Liquid With Basic Lead Acetate

After extraction of the original aqueous liquid with ether, it was treated with an excess of basic lead acetate in the usual way, the liquid being vigorously stirred with an electric stirrer during the addition of the lead solution. This produced an abundant, dense yellow-brown precipitate. The precipitate was allowed to settle, the supernatant portion siphoned off and the sludge filtered in a large Buchner funnel. The precipitate was suspended in water, stirred and separated as before and thoroughly washed with water on the funnel. The aqueous portion now amounted to about eight liters and was reserved for further examination.

Basic lead acetate precipitate. The precipitated lead compound was suspended in water, stirred and decomposed by a stream of hydrogen sulphide. The lead sulphide was allowed to settle, the liquid siphoned off and the residue filtered on a Buchner funnel. After thoroughly washing the lead sulphide with hot water, the excess of hydrogen sulphide was removed from the filtrate by a current of carbon dioxide. A test of the boiled filtrate readily reduced Fehling's solution and when warmed with solid sodium hydroxide an ammonia-like odor was produced.

The clear, dark-colored aqueous liquid was concentrated under reduced pressure to about two liters.

Isolation of Glucose [7]

Preliminary tests showed that a quantity of material separated on the addition of acetone, hence an equal volume of acetone was

[7] The basic lead acetate treatment was expected to leave the "sugars" in the filtrate. Instead all the reducing substances present were carried down by the lead precipitate, probably by occlusion and may be accounted for by the large amount of precipitate as compared with the small amount of reducing substances. Cp. Browne, C. A., *A Handbook of Sugar Analysis,* New York, 1912, p. 215.

added. The precipitated material was allowed to settle, filtered and amounted to slightly less than 3.0 gms. It rapidly reduced Fehling's solution and gave a positive test with Molisch's reagent. Hence the dark precipitate was treated with phenyl hydrazine hydrochloride in the usual way. This yielded a small amount of an osazone, which after crystallization melted at 199-201 degrees with decomposition. When mixed with an authentic sample of glucosozone it showed no depression. Since glucose is most commonly met with in plant material, the carbohydrate may be considered as such.

The filtrate from the acetone precipitation still gave a strong positive test with Fehling's solution. The acetone was removed by distillation from a steam bath and the aqueous liquid was further concentrated under pressure to a volume of 150 cc. Besides the reducing substances present, there were indications of some acid, other than acetic acid present. The solution yielded a deep red color with ferric chloride and gave a red color with green fluorescence when treated with resorcinol and sulphuric acid. This color test is shown by acids of the fatty acid series which give internal anhydrides as well as the orthodecarboxylic acids of the benzene series.[8] Accordingly the aqueous liquor was again treated with basic lead acetate, the lead precipitate and the filtrate worked up as described below.

Isolation of Succinic Acid

The almost white precipitate produced by the basic lead acetate was suspended in a large volume of water, and electrically stirred. Dilute sulphuric acid (1:5) was added very slowly until a slight excess had been added as shown by repeated tests on filtered portions. The residual lead in solution was removed by hydrogen sulphide. The precipitate of lead sulphate and lead sulphide were filtered off and washed with hot water until neutral to litmus. The filtrate, which now had a slight brownish color, was decolorized with charcoal. The colorless filtrate was evaporated under reduced pressure to a small volume and then set aside for spontaneous crystallization, when a small amount (about 0.5 gm.) of a perfectly white substance separated. After drying over sulphuric acid it melted at 183-184 degrees. Titration—also analysis of the silver salt, prepared through the ammonium salt, showed the substance to be succinic acid.

[8] Rosenthaler, L., *Nachweis Organischer Verbindungen,* Stuttgart, 1914, p. 330. Cp. Power, F. B., and Chestnut, V. K., *J. Am. Ch. Assoc.,* 1926, XLVIII, 2726.

0.1000 gm. subs. required 16.89 cc. 0.1 N KOH. Theory for $(CH_2COOH)_2$ requires 16.94 cc.

0.1047 gm. silver salt (dried at 110°) yielded 0.0683 gm. Ag

Calc. for $(CH_2COO\ Ag)_2$	Found
65.0 per cent. Ag	65.3

Isolation of a Methyl Pentose

As previously mentioned, the liquid after the separation of the acetone insoluble substances strongly reduced Fehling's solution. Hence the acid filtrate from the last lead treatment was neutralized with 10 per cent. sodium carbonate solution and then concentrated under pressure to a volume of about 75 cc. The dark brown liquid was transferred to a crystallizing dish and allowed to evaporate over sulphuric acid in a vacuum desiccator. This yielded about 17 gms. of a dark, brown syrup with a sweet taste. Ten gms. of the syrup were used for the preparation of an osazone. Phenylhydrazine and glacial acetic acid were added to the aqueous solution and refluxed for forty-five minutes. A small amount of a dark yellow micro-crystalline material, accompanied by some tarry material, was obtained. After filtering, the product was stirred with benzol and again filtered. This treatment removed most of the tarry material. The residue, after crystallization from dilute alcohol, melted at 178 degrees with decomposition. On account of the small amount only a nitrogen analysis was made.

0.1327 gm. subs. yielded 19.5 cc. nitrogen at 26° and 746 mm.

Calc. for $C_{18}H_{22}O_3N_4$	Found
16.37 per cent. N_2	15.9

Rhamnose phenyl-osazone melts at 180 degrees.[9]

Filtrate from the Basic Lead Acetate Precipitation. The filtrate from the original basic lead acetate precipitation measuring about ten liters was concentrated under reduced pressure to about two liters and the excess lead removed by a stream of hydrogen sulphide. The lead sulphide was washed several times with hot water and discarded, the washings being added to the main portion, from which the dissolved gases were removed by a stream of carbon dioxide. The light brown liquid was further concentrated under reduced pressure to approximately 300 cc., whereupon a further quantity (14

[9] Ref. 8, p. 189.

gms.) of potassium nitrate settled out. The filtrate, after removal of the inorganic salt, was treated with two volumes of 95 per cent. alcohol and allowed to stand overnight, whereupon a further quantity (20 gms.) of potassium nitrate settled out. The alcohol from the filtrate, after the removal of the potassium salts, was recovered by distillation from a water bath.

The dark brown solution, when acidified with sulphuric acid, responded to the usual alkaloidal tests. These reactions were evidently due to the presence of betaine and choline, which were subsequently isolated. The solution yielded a negative test with Fehling's solution before hydrolysis, but reacted strongly positive after hydrolysis with hydrochloric acid, thus indicating the presence of compounds of a glucosidic nature, which, however, were not isolated.

The acid liquid was neutralized with a 10 per cent. solution of sodium carbonate and sulphuric acid (1:1) added until a 10 per cent. solution was reached. The acidified liquid was extracted successively with ether, chloroform and hot amyl alcohol. Nothing of interest was removed by these solvents.

The solution was now made alkaline with sodium hydroxide and extracted with chloroform and hot amyl alcohol. Nothing was removed, hence the absence of alkaloids may be assumed.

Isolation of Betaine and Choline [10]

The aqueous liquid after the series of operations just described was acidified with sulphuric acid and a saturated solution of phosphotungstic acid added, when a very abundant precipitate was obtained. The precipitate was collected on a Buchner funnel and the filtrate reserved for further examination. The precipitate was washed with hot water and the washings added to the main portion. The precipitate was decomposed with a saturated solution of barium hydroxide, and the mixture filtered, after which the excess barium was removed from the filtrate by a current of carbon dioxide. The barium carbonate was filtered off and the filtrate concentrated under diminished pressure to the consistency of a syrup. The latter was extracted six times with 50 cc. portions of alcohol. To the filtered alcoholic liquid a cold saturated alcoholic solution of mercuric chloride was added, and the mixture allowed to stand eighteen hours, when a light brown crystalline material settled. This was collected by suction filtration and dried on a porous plate. Thus treated it amounted to 9 gms.,

[10] Barger, G., *The Simpler Natural Bases*, London, 1914, p. 116.

7 gms. more were obtained by concentrating the filtrate to one-half. The solid was dissolved in 600 cc. of hot water and the solution treated with hydrogen sulphide for the removal of mercury. After filtration, the excess of hydrogen sulphide was removed by a stream of air. The absence of purine bases and of arginine was indicated by negative tests, when silver and mercury nitrates respectively were added to the solution acidified with nitric acid.

After removal of the mercury, the colorless filtrate was concentrated under diminished pressure to a small volume (about 120 cc.) and the further evaporation was conducted in a vacuum desiccator over solid potassium hydroxide. After some days the small quantity of crystals which had separated was collected on a small Buchner funnel and washed with absolute alcohol, the filtrate being reserved for the examination for choline. The quantity of crystals which separated amounted to 4.1 gms., which corresponds to 0.03 per cent. of the leaves. After drying on a porous plate in a desiccator over solid potassium hydroxide, the material melted sharply at 234-235 degrees with slow heating, which indicates it to be betaine hydrochloride. This was confirmed by the preparation of the chloro-aurate and the examination for chlorine and nitrogen.

0.2000 gms. subs. by the Kjeldahl-Gunning method gave NH_3 equivalent to 13.07 cc. 0.1 N HCl.

0.2009 gms. subs. yielded 0.1869 gms. AgCl.

Calc. for $C_5H_{12}O_2NCl$	Found
N 9.12	N 9.15
Cl 23.1	Cl 22.98

0.1564 gms. subs. yielded 0.0671 gms. Au.

Calc. for $C_5H_{12}O_2N$. Au Cl_4	Found
Au 43.13	42.90

The alcoholic washings from the betaine were evaporated to a small volume and treated directly with an aqueous solution of chloroplatinic acid. The crystalline deposit, after filtering, washing with alcohol and drying at 110 degrees, was analyzed.

0.0872 gms. subs. yielded 0.0275 gms. Pt.

Calc. for $(C_5H_{14}ON)_2$ Pt Cl_6	Found
Pt 31.67	31.54

Filtrate from the Phosphotungstic Acid Precipitation. The light green-colored filtrate from the phosphotungstic acid precipitation

measured about two liters. The excess of phosphotungstic and sulphuric acids was removed by barium hydroxide and the excess of base in turn removed as the carbonate. It slightly reduced Fehling's solution after hydrolysis. The liquid was concentrated under reduced pressure to a small volume, whereupon a quantity of crystalline material separated. It was found to be a mixture of barium and sodium acetate. The aqueous alcoholic liquor was further evaporated to a syrup. Crystallization from various solvents was to no avail, hence the syrup was hydrolyzed with 5 per cent. hydrochloric acid. Extraction with ether and steam distillation failed to remove the aglycon. A very small amount of an osazone, melting at 187-188 degrees, was obtained in the usual way. It was not further examined.

Examination of the Resin (B)

The previously mentioned black, oily resin which had been thoroughly washed with water, was mixed with purified sea sand and the mixture thoroughly dried on the steam bath. The mixture was exhaustively extracted in the following manner: The magma of sand and resin was transferred to a large, hard glass bottle, the solvent added and vigorously shaken on a shaking machine. The spent solvent was filtered from time to time, recovered by distillation and returned to the bottle. This extraction was carried out with the solvents in the order named below.

Petroleum-Ether Extract. Petroleum ether (B. P. 30-75°) was first used. This yielded after complete removal of the solvent 972.0 gms. or 6.9 per cent. of the dried leaves of a black semi-solid oil.

Ether Extract. The material which had been extracted with petroleum ether was placed on a radiator until no odor of petroleum ether was apparent and then extracted with ether. The last traces of solvent from the ethereal solution were allowed to evaporate spontaneously, thereby yielding a fine, green-colored powder which amounted to 75.0 gms. or 0.57 per cent. of the dried leaves.

Chloroform Extract. This and the subsequent extractions were carried out in a large improvised Sohxlet apparatus. The chloroform extraction yielded 85 gms. or 0.6 per cent. of the dried leaves, of a hard, brittle, black substance.

Ethyl Acetate Extract. The extraction yielded 15 gms. of a black powder.

Alcoholic Extract. The extraction yielded 15 gms. of a black powder.

Petroleum—Ether Extract of the Resin

The entire amount of the petroleum ether extract, amounting to 972.0 gms., was saponified by heating for six hours on a water bath with 300 gms. of potassium hydroxide dissolved in three liters of alcohol.[11] The alcohol recovered by steam distillation reacted alkaline to litmus, hence the alcoholic distillate was collected in dilute hydrochloric acid. The alcohol was distilled from the acid liquor and the residue evaporated to dryness, yielding a small amount of a dark, semi-crystalline residue, which was purified by dissolving in water and boiling with charcoal. The clear filtrate on slow evaporation yielded a small amount of a hygroscopic salt, which was converted directly into a chloroplatinate.

Identification of Methylamine and Ammonium Chloride

By fractional precipitation two portions of the chloroplatinate were obtained; the first weighing 0.23 gm., the second 0.26 gm. After drying at 110 degrees they were analyzed.

0.0918 gm. subs. yielded 0.0380 gm. Pt

Calc. for $(CH_3NH_2)_2PtCl_6$	Found
Pt 41.35	41.39

0.1354 gm. subs. yielded 0.0598 gm. Pt
0.1217 " " " 0.0537 " "

Calc. for $(NH_4)_2PtCl_6$	Found	
Pt 43.96	44.31,	44.12

To the strongly alkaline mixture a quantity of washed sea sand was added and the whole heated on the water bath for the removal of residual water. After having been thoroughly dried the mixture was extracted by digestion with ether, the ethereal solution washed with water and the washings used to dissolve the potassium soaps present in the sand. The aqueous solution of soaps and glycerol (about 18 liters) was extracted with three 500 cc. portions of ether and the

[11] Twice the amount of alkali as calculated from preliminary saponification data was used.

ether added to the main ethereal solution of non-saponifiable constituents.[12] The aqueous solution was reserved for further examination.

After drying the ethereal solution over anhydrous sodium sulphate, the solvent was removed by distillation, the last traces being removed by a current of air.

Unsaponifiable Constituents of the Petroleum Ether Extract

The above-mentioned united ethereal extracts yielded a dark red, semi-solid product. Since preliminary saponification tests had shown that a compound of a volatile nature was set free by the alkaline hydrolysis, the dark-colored mass was steam-distilled. This treatment yielded 34.0 gms. of a light yellow oil with an odor slightly different than that of the original volatile oil. Since this oil, evidently of an alcoholic nature, was obtained only after the alkaline hydrolysis of the "fatty acid" material, it is suggested that the alcohol may originally have been present as an ester of a higher fatty acid, non-volatile with steam. The occurrence of such a large amount of oil (almost 30 per cent. of the original volatile oil) at this point further suggests the possible economic losses involved in the ordinary method of producing these products by direct steam distillation of the herb. From the biochemical viewpoint such losses are too significant to be overlooked, as they may lead to serious errors in tracing the biogenetic relations of the compounds present in a plant.[13, 14]

After drying over anhydrous sodium sulphate, the physical constants were:

$n_D^{20°}$ 1.4695

$D(\frac{20°}{20°})$ 0.8787

$[a]_D^{20°}$ 1.06

Phenols and certain sesquiterpenes were absent as shown by color tests with ferric chloride and acetic and sulphuric acids respectively. Acetylization and consequent saponification showed 55.8 per cent. alcohol calculated as $C_{10}H_{18}O$.

[12] The removal of the non-saponifiable constituents by the method described has been found more satisfactory than extraction of the strongly alkaline solution with ether. Disagreeable emulsions are thus avoided.

[13] Kremers, R. E., ref. 3.

[14] Kremers, R. E., *J. Am. Pharm. Assoc.*, 1921, X, 252.

Isolation of Linalool $C_{10}H_{18}O$

The volatile oil (29.5 gms.) obtained as already described was subjected to distillation under reduced pressure with the following results:

Fraction	Temp.	Gms.	$n_D^{20°}$	$D_{20°}^{20°}$	$(a)_D^{20°}$
1	88-100/16 mm.	8.5	1.4599	0.8629	—6.37
2	88-100/10 mm.	9.3	1.4641	0.8696	—1.61
3	100-110/10 mm.	7.0	1.4719	0.8761	+3.13
4	110-120/10 mm.	2.8	1.4778	0.8895	—
5	120-140/10 mm.	Few drops	—	—	—
6	Residue	2.0	—	—	—

The physical constants indicate the bulk of the oil to be linalool.[15]

Attempts to prepare the phenyl and α-naphtyl urethanes led in every case to the formation of the corresponding diarylureas. However, since linalool is known to be isomerized to geraniol by acids, the method developed by Power [16] was satisfactorily used for the identification of linalool from the first three fractions. Tests for acetone and levulinic acid were readily obtained. After the greater part of fractions 1 and 2 had been oxidized with chromic acid mixture,[17] citral was identified as α citryl β naphthochinonic acid melting at 198-200 degrees. When mixed with a similar preparation from an authentic sample of linalool, no depression was noted.

After the steam distillation of the unsaponifiable matter, the residue was separated from the water with ether, the ethereal solution washed, dried and the solvent removed. This yielded 205 gms. of a waxy semi-solid mass accompanied by a red oil, which in dilute ether solution was light yellow.

The entire product was then treated with 500 cc. alcohol, cooled and in ice. This treatment yielded 28 gms. of a waxy semi-solid material, still accompanied by the red oil. A repetition of the above alcoholic treatment gave an almost white product, which was further purified by alcohol and charcoal. All the alcoholic liquors were bulked for subsequent examination. The white substance amounting to about 10 gms. melted at 60-75 degrees and gave the color reactions charac-

[15] Stephan, K., *J. prakt. Chem.*, 1898, LVIII, 110.
[16] Power, F. B., and Chestnut, V. K., *J. Am. Ch. Soc.*, 1922, XLIV, 2939.
[17] Bertram, J., and Walbaum, H., *J. prakt. Chem.*, 1892, XLV, 599.

teristic of the sterols. It was separated into two portions by means of acetic anhydride.[18]

The above-mentioned solid substance had an appearance suggestive of candle wax and was accordingly twice treated with 30 cc. of acetic anhydride. About half of the material dissolved, while the rest floated on the surface. This was separated by filtration through a steam funnel, kept warm but not hot.

Isolation of a Paraffin Hydrocarbon, Dotriacontane

The portion insoluble in acetic anhydride was dried on a porous plate, then purified successively from benzene, absolute alcohol and charcoal and filtered through a hot water funnel. On cooling, the substance settled as a white waxy mass. This was collected on a suction filter, washed with alcohol, and dried on a porous plate in a desiccator over sulphuric acid. It weighed 3.0 gms. and was not affected by conc. sulphuric and nitric acids nor did it decolorize a 1 per cent. permanganate solution and reacted negatively to the sterol tests. It melted sharply at 69.5-70 degrees. All these characters indicate it to be a hydrocarbon, *viz.*, dotriacontane.[19] This was confirmed by analysis.

0.1284 gm. subs. yielded 0.3910 gm. CO_2 and 0.1640 gm. H_2O.

Calc. for $C_{32}H_{66}$	Found
C 85.33	85.41
H 14.66	14.54

The identity of the substance as dotriacontane is thus established.

(To Be Continued.)

FIRST AID METHODS FOR TREATING THE INJURED

Prepared Under the Direction of the Surgeon General, United States Public Health Service

THE UNITED STATES PUBLIC HEALTH SERVICE advises that everyone become familiar with first-aid methods for treating the injured. First-aid has been defined as the temporary care of an injured person by simple, commonsense methods, based on

[18] Benedikt, R., and Ulzer, F., *Analyse der Fette und Wachsarten*, 4th Ed., Berlin, 1903, p. 269.

[19] Krafft, F., *Ber. Chem. Ges.*, 1886, XIX, 2218.

principles of medicine and surgery, that may be applied easily by persons not professionally trained in those subjects. *It should be noted that the work of first aid ceases when the injured person has been turned over to the care of a physician.**

When it is remembered that over 28,000 persons are killed in the United States each year by traffic accidents—that is, by automobile, railroad, street car accidents, etc.—over 13,000 by falls, more than 6000 each by burns and drowning, and more than 27,000 by other accidental means, or a total of more than 80,000 persons killed and over two million additional seriously injured by accidents in the United States each year, the importance of first-aid care is at once obvious. The above does not include the minor injuries, for which there are no statistics at the present time.

The common injuries include wounds with bleeding and possible infections, dislocation and fracture of bones, burns, including those caused by chemicals, and asphyxia, or cessation of respiration. The principles upon which first-aid are based are as follows:

First, cleanliness in caring for all open wounds. Persons administering first-aid should be instructed not to touch or put anything on open wounds except a dry sterile compress or bandage compress. A bandage compress, which consists of several thicknesses of sterile gauze sewed to the middle of a strip of muslin, is used to cover all open wounds. Three sizes of compresses are used—large, medium, and small. The compress should usually be covered by a protective dressing. A triangular bandage has been found very suitable for this purpose, as it can be adapted to cover any part of the body. The triangular bandage is used either in the open form or folded cravat. In addition to being used to protect the other dressings, it may be used as an improvised tourniquet and to hold splints in place. A triangular bandage may be made from any kind of cloth such as a handkerchief, piece of shirt, or napkin. It has been found, however, that a piece of muslin forty inches square, folded diagonally and cut

*Editor's Note: Attention is called to the fact that unscrupulous persons have taken advantage of kindly acts to secure damages from those whose sympathies and humanity persuaded them to give aid. The charges in the cases in mind were technical and not all persons adhere to the truth when their desire for money gets the better of them. Members of the A. Ph. A. will find reference to cases in May Journal A. Ph. A., p. 485. A firm, known to the writer, had a related experience many years ago in which permanent injury was alleged, but fortunately (disastrously for the plaintiff and his attorneys) the attempted deception was uncovered by a special jury of physicians. The comment is made so that pharmacists will be guarded in their actions.

across the long side, making two triangular bandages, is most satisfactory.

The second principle in first-aid is the control of hemorrhage, or bleeding. Hemorrhage from a cut artery flows rapidly in spurts or fine jets, giving little time for the blood to coagulate or clot. The blood is bright red. Blood from a vein, being under less pressure, flows steadily, but it may be rapid if from a large vein. It is dark red in color. Bleeding from small arteries can often be controlled by direct pressure, but it is generally best to apply a tourniquet immediately, between the wound and the heart. Bleeding from a vein can usually be stopped by simply pressing a pad of sterile gauze over the wound and then elevating the part, having the patient lie down. Anything that makes the heart beat faster increases hemorrhage; hence in all cases of severe bleeding the patient should be kept in a recumbent or semi-recumbent position and as quiet as possible.

The third principle is the restoration of breathing after electric shock, apparent drowning, and poisoning by gases, as by carbon monoxide gas or illuminating gas. This treatment is by artificial respiration. Any method of artificial respiration may be used. For the ordinary person rendering first-aid. the Schaefer, or prone pressure, method is the simplest and is not as tiresome as some of the other methods. Recently a conference was held at which representatives of the United States Public Health Service, the United States Bureau of Mines, the American Red Cross, and other national organizations were present, for the purpose of deciding upon a uniform technique. This technique is very simple and anyone can learn it in a short time. It is as follows:

(a) Lay the patient on his belly, one arm extended directly overhead, the other arm bent at elbow and with the face turned outward and resting on hand or forearm so that the nose and mouth are free for breathing.

(b) Kneel straddling the patient's thighs with your knees placed at such a distance from the hip bones as will allow you to place the palms of your hands on the small of the patient's back with your fingers resting on the ribs, the little finger just touching the lowest rib, with your thumb and fingers in a natural position, and the tips of your fingers just out of sight.

(c) With your arms held straight, swing forward slowly so that the weight of your body is gradually brought to bear upon the patient. Your shoulders should be directly over the heel of your

hand at the end of the forward swing. Do not bend your elbows. This operation should take about two seconds.

(d) Now immediately swing backward so as to completely remove the pressure, thus returning to the first position.

(e) After two seconds, swing forward again. Thus repeat deliberately twelve to fifteen times a minute the double movement of compression and release, a complete respiration in four or five seconds.

(f) Continue artificial respiration without interruption until natural breathing is restored or until a physician declares the patient is dead.

(g) As soon as this artificial respiration has been started and while it is being continued, an assistant should loosen any tight clothing about the patient's neck, chest, or waist. Keep the patient warm. Do not give any liquids whatever by mouth until the patient is fully conscious.

(h) To avoid strain on the heart when the patient revives, he should be kept lying down and not allowed to stand or sit up. He should be given some stimulant, such as one teaspoonful of aromatic spirits of ammonia in a small glass of water or a hot drink of coffee or tea. The patient should be kept warm.

(i) Resuscitation should be carried on at the nearest possible point to where the patient received his injuries. He should not be moved from this point until he is breathing normally of his own volition and then moved only in a lying position. Should it be necessary to move the patient before he is breathing normally, resuscitation should be carried on during the time that he is being moved. A brief return of natural respiration is not a certain indication for stopping the resuscitation. Not infrequently the patient, after a temporary recovery of respiration, stops breathing again. The patient must be watched and if natural breathing stops, artificial respiration should be resumed at once.

(j) In carrying out resuscitation it may be necessary to change the operator. This change must be made without losing the rhythm of respiration. By this procedure no confusion results at the time of change of operator and a regular rhythm is kept up.

The fourth principle relates to dislocations and fractures of bones, which are treated by immobilization in a comfortable position, and a natural one if practicable, care being taken not to move the injured part unnecessarily. Well-padded splints are held in place by cravat bandages.

Fifth, burns are treated, after removal of the clothing, by use of sterile or sterile picric acid gauze and an outer dressing, as a triangular bandage, to hold the gauze in place and exclude the air. The exclusion of air is important. Precautions of cleanliness should be observed as stated for open wounds.

Sixth, shock, or vital depression, which accompanies all injuries to some degree, is treated by keeping the patient lying down at rest; keeping him warm by covering him wth blankets or clothing, using hot water bottles, hot bricks, or similar means, aiding circulation by rubbing the extremities towards the heart, but not away from it; and by the use of common stimulants, as hot coffee or aromatic spirits of ammonia.

Seventh, transportation may be necessary to get an injured man to a place of safety, or to a more comfortable location, or to get him to a hospital and a physician. The methods vary with conditions, but the principle of transporting him so that he will suffer no further injury is important, whether he is transported on a stretcher or by one, two, three or more persons.

In summarizing, the most important thing in the care of the injured person is PREVENTION—the reduction of accidents to a minimum by education and legislation. But as this minimum can never be zero, it is well to bear in mind the fundamental principles in first-aid care, which are as follows:

1. Asepsis or cleanliness in caring for open wounds.
2. Control of hemorrhage by pressure and position of injured part.
3. Treatment of shock by keeping patient at rest and warm and by giving simple stimulants.
4. Artificial respiration in asphyxia, electric shock, combined with the use of pure oxygen in carbon monoxide cases.
5. Asepsis in treatment of burns; protection from air if this can be done with aseptic method; antisepsis and some relief of pain by use of picric acid gauze.
6. Immobilization of dislocations and fractures.
7. Transportation by methods that will not increase the extent of the injury.

In addition to the benefits gained by the early care of the injured, first-aid has been found actually to tend to lower accidents by making people more careful.

CHEMICAL CHARACTERIZATION OF DRUGS[1]

By L. Rosenthaler, Berne

THE CHARACTERIZATION OF DRUGS in a chemical way, can, in many cases be done with the drug itself, as with strophanthus seed by the detection of strophanthin (color reaction with concentrated sulphuric acid), with opium by the detection of morphine (with formaline-sulphuric acid), of narcotine (with arsenic sulphuric acid), or of meconic acid (with ferric sulphate). In the majority of cases the substances, with the help of which it is intended to characterize the drug, must be previously separated, even if in an impure condition. For this purpose sublimation or extraction may be employed. These procedures are set forth in publications already issued by *Tunmann* and myself. In the case of sublimation different methods may be used, depending on whether we operate in vacuum or not. In the case of extraction the solvent must be selected in conformity with the substance to be extracted. For extraction of alkaloids ammoniacal-chloroform is recommended but *pulpa tamarindi* is to be extracted with water. In those cases in which the extraction is made with a solvent that does not mix with water, it is often advantageous, especially when extracting fine powders, to moisten them beforehand on the slide with water. In such cases apply the cover-glass, incline the slide and fill up the space between the cover-glass and the slide with the solvent. After the latter has evaporated the extracted body is found at the edge of the cover-glass or nearby.

A number of examples of the chemical characterization of drugs, are here given for which the extractive method was mostly employed.

Pulpa Tamarindi. The most important ingredient of *pulpa tamarindi* is tartaric acid, which is present partly in a free state and partly as a potassium salt. To test, triturate a small amount of the pulp on a slide with water, remove the watery extract with a glass rod and then add a few small grains of calcium acetate. The calcium tartrate that results, forms first spherules and then spherocrystals. It may remain in this latter condition but can pass into a modification of the rhombic octahedron. In order to test for potassium, the well-known compound of potassium-copper lead ni-

[1] From *Pharmaceutica Acta Helvetiæ*, April 24, 1926.

trite may be used. Upon a slide place a drop of sodium nitrite solution with a drop of a solution of copper and lead acetate and then add a small particle of tamarind pulp. After a while, at the edge, the black cubes of potassium copper-lead nitrite may be observed.

Piper Nigrum. Various methods [2] of procedure have been proposed for the detection of piperin, all of which have the object to isolate the piperin by means of a solvent or by means of sublimation without making any further identification of it. For extraction we obtain the best result with chloroform for identification, by means of a cadmium compound of piperin. If to the solution of the piperin in a small quantity of concentrated hydrochloric acid, we add a little solid cadmium acetate or sulphate there will appear soon a turbidity

Diagram 1—Calcium tartrate

of (little grains or little drops) yellow needles (diagram 2) in part isolated and in part in sheaves and bunches.[3] The best way to proceed is therefore as follows:

Extract a little pepper powder on the slide with chloroform. After this has evaporated piperin prisms appear chiefly at the edge. Brush the edge over with concentrated hydrochloric acid, even if piperin crystals are not yet to be seen. Introduce into the fluid some small crystals of cadmium acetate or sulphate. The yellow needles of the piperin cadmium compound, described above, appear quickly.

[2] See O. Tunmann, Pflanzenmikrochemie, page 283.

[3] These crystals must not be confounded with the colorless spears which occasionally are to be seen, especially at the edge of the drop, and which are probably cadmium chloride.

We can also conduct the experiment by stirring a little pulverized pepper up with hydrochloric acid and adding the cadmium salt to it.

Cortex Cinnamonii. Among the constituents of the volatile oils, available for identification, it is only cinnamin aldehyde that can be used for characterization of cinnamon. All of our attempts to test for it directly in pulverized cinnamon have been without success. It has happened occasionally that we thought that we had obtained a crystalline structure with semioxamacid, but this was not always the case.

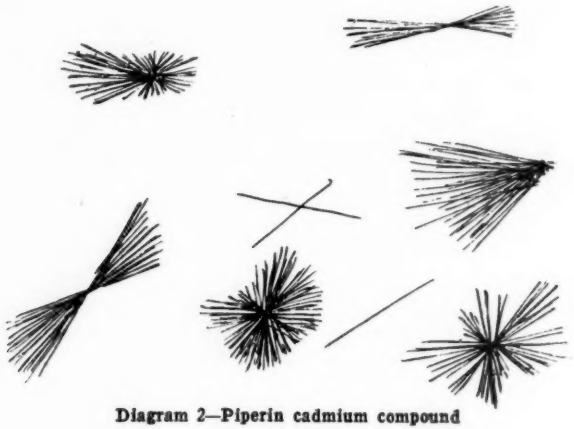


Diagram 2—Piperin cadmium compound

The best procedure is to extract the volatile oil with chloroform. After the evaporation of this, a solution of phenylhydrazin hydrochloride (1:10) is placed between the cover-glass and the slide, in the layer at the edge the little rods of the cinnamic aldehyde-phenylhydrazone appear. This reaction can also be obtained in the sublimate.

Caryophyllus

In cloves, eugenol serves for identification. *H. Molisch* recommended transforming it into the needles of potassium eugenol by a saturated solution of potassium hydroxide. The reaction is not always positive with slices of cloves, but crystalline structures will be produced, if a 3% solution of sodium hydroxide, saturated with sodium bromide is used,[4] for the test. On slices through cloves

[4] Van Urk, *Pharm. Weekblad*, 62, 667.

we obtain with this test in the reservoirs of secretion, or near them, numerous needles of sodium eugenol. Also in the pulverized cloves they may be occasionally observed. It is better to extract first with chloroform. After the evaporation of the latter we put the reagent between the slide and the cover-glass, there will appear *immediately* at the edge numerous needles, often in a bush or shrub arrangement.

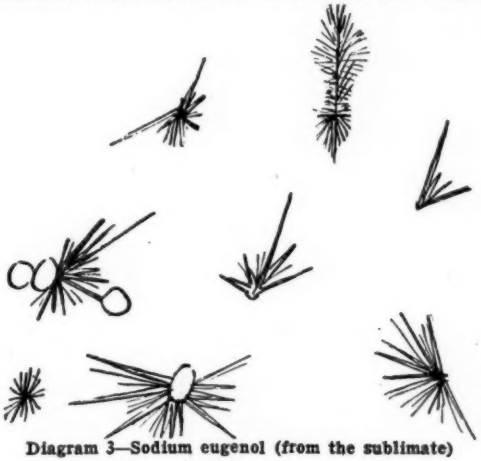


Diagram 3—Sodium eugenol (from the sublimate)

Diagram 4—Carophyllin (sublimate)

The reaction takes place also very nicely if we first sublime and treat the sublimate with the reagent. The crystals (diagram 3) are developed out of the drops. If we continue to heat pulverized cloves until carbonization begins there will be seen beside the blackened particles numerous bunches, needles of caryophyllin, which give a sublimate of bush-shaped entangled needles (diagram 4) as well as little grains. *Clove stems* act exactly like the cloves.

Flos Cinæ. The strong red coloration, which santonin gives with alcoholic potash, is not suitable for identifying the drug itself, inasmuch as *Flos Cinæ,* free from santonin, will also give an orange coloration with this reagent. *O. Tunmann*[5] called attention to this fact and we can confirm it. If we treat the moistened powder on the slide with chloroform. The residue after evaporation will give with alcoholic potash a strong orange-red coloration—not such a clear red as with pure santonin, if genuine *Flos Cinæ* are to be identified. Specimens free from santonin gave only a yellowish-green.

Semen Myristicæ. An extraction of nutmeg powder on the slide with chloroform will give on the edge after the evaporation of the chloroform numerous needles arranged in bunches (diagram 5), which show strong polarization between crossed Nicols, and can in this way be detected. Inasmuch as the crystals are soluble in water

Diagram 5—Groups of crystals from Semen Myristicae and Macis

it might be a question of a phenol or an acid, perhaps a fatty acid (myristic acid[?]). If we add to the preparation a solution of phloroglucinol in strong hydrochloric acid (1.19), the border layer, in which the crystals lie, gradually becomes red. It is well known that among other substances, those with an allyl group give this reaction and as the myristicin contains an allyl group, the reaction may be attributed to this.

Macis. This acts as *Semen Myristicæ.*

Amygdala Amara. For the chemical characterization here we make use of the test for hydrocyanic acid and benzaldehyde, which are developed in the well-known reaction by the addition of water.

For the test for hydrocyanic acid we employ the decoloration of iodized starch, as previously stated.[3] We can also proceed as follows for the detection: Put a small portion of crushed almonds in a

[5] Pflanzenmikrochemie, page 249.

[3] *Schweizerische Apotheker-Zeitung,* 60 (1922), No. 35.

Molisch glass chamber [7] (see diagram 6), add a drop of water and then cover with a small cover-glass which bears on its inside a drop of 1 per cent. silver nitrate solution, that has been slightly colored with methylene blue. After the drop has become cloudy, replace the cover-glass by another that bears on the inside a drop of a 5 per cent. solution of phenylhydrazin hydrochloride, and after this has again become cloudy it is replaced by a cover-glass bearing on the inside hydrazin sulphate solution (equal parts of a saturated solution and water).

On the first cover-glass, blue needles of silver cyanide will be formed; on the second small rods of benzal-phenyl hydrazone, which gradually become larger; on the third, needles and little rods will appear, which in part lie isolated and in part can combine to form structures shown in diagram 7. Here it is probably a question of aldazin.

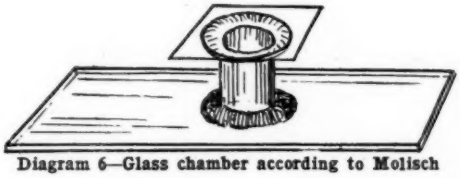


Diagram 6—Glass chamber according to Molisch

Semen Sinapis Albæ. The white mustard seed contains sinalbin, among the cleavage products of which sinalbin oil or p-oxy-benzyl mustard oil.

$$C_6H_4\begin{cases}OH\,(1)\\CH_2NCS\,(4)\end{cases}$$

It was assumed that this would give a red with Millon's reagent, as all similarly constituted substances do. On this the following test is founded: Moisten 0.25 gm. of white mustard meal with water in a test tube. After at least fifteen, or better thirty, minutes shake with a few cc. of petroleum ether and allow this after filtration through a double filter to evaporate spontaneously. The residue gives an intense red with Millon's reagent, while a control test, conducted in the same manner, except without moistening with water, gives either no red or only a light one.

[7] The glass chamber can be made by fastening the split-off neck of a little medicine vial with sealing wax on a slide.

Semen Sinapis Nigræ. The sinigrin of black mustard is just as little suited for the direct test as that white mustard. We must, therefore, base the test on the allyl mustard oil, which originates through enzymic action. The allyl mustard oil may be tested by different reactions, for example, by ammonia (forming thiosinamin) or by phenylhydrazin. With the latter reaction A. Pietschmann [8] could detect 0.01 milligram (?) of mustard oil after an action of twelve to twenty-four hours. The formation of a precipitate with

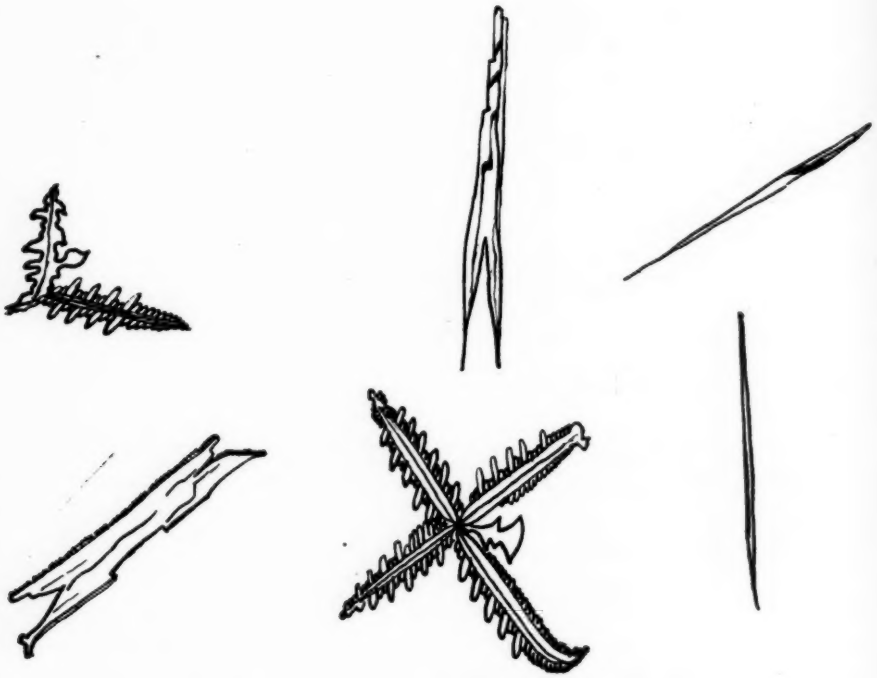


Diagram 7—Combination of benzaldehyde and hydrazin

bromine water is also very sensitive. We can oxidize the allyl mustard oil with potassium permanganate and test for sulphuric acid with barium chloride, proceeding as follows: Moisten 0.05 gm. of ground mustard in the Molisch glass chamber with a little water, then cover with a cover-glass, on the inside of which there is hanging a drop of a 1 per cent. solution of permanganate acidulated with hydrochloric

[8] *Zeitschrift für Mikrochemie,* II, 33 (1924).

acid, and after ten minutes heat with a small flame of a microburner. After five minutes remove the cover-glass, mix the permanganate solution with a drop of hydrochloric acid. Cause the permanganate and manganese dioxide to disappear by light heating over the microburner. Let a drop of barium chloride solution flow into it, turbidity will be produced.

It is evident that we can test in this manner not only all volatile mustard oils but especially all volatile sulphur compounds which form sulphates with permanganate.

It is therefore advisable to complete a test by that with phenylhydrazin. We proceed as is indicated above, but we must put on the

Diagram 8—Combination of arbutin and p-nitrosodimethylaniline

inside of the cover a little drop of phenylhydrazin. In twelve to twenty-four hours there will then be needles of an additional combination which will appear much more clearly defined after treatment with alcohol, in which it is insoluble.[9]

Fol. Uvæ Ursi

Arbutin, the chief constituent of bearberry leaves, gives a very characteristic reaction with nitrosodimethylaniline: If we add to a freshly-prepared solution [10] of p-nitrosodimethylaniline a small grain of arbutin, then there will be gradually formed deep orange-red nodules and stars, composed of little rods (see diagram 8); during the

[9] Pietschmann 1, c.

[10] 0.2 Gm. p-nitrosodimethylanilinhydrochloride, 0.15 Gm. sodium acetate, 10 Gm. of water, filter.

evaporation tree-like forms of the same color appear originating from the edge.[11]

Unfortunately the reaction cannot be used to identify arbutin in leaves, as the tannin is a disturbing substance. Nor can the orange-red that arbutin gives with Millon's reagent be of any use. We are obliged to identify the hydroquinone, the aglycon of arbutin, as *O. Tunmann* did. Tunmann lets the hydroquinone sublime after previous treatment with diluted sulphuric acid or emulsion, but we can dispense with this preliminary treatment. If we heat arbutin on the asbestos plate, it decomposes and yields a sublimate of hydroquinone.

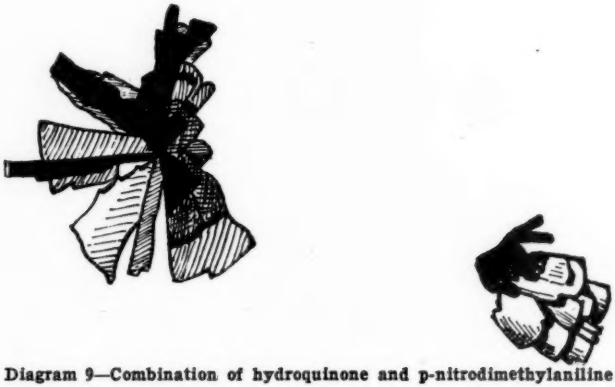


Diagram 9—Combination of hydroquinone and p-nitrodimethylaniline

Correspondingly, we obtain immediately a sublimate of hydroquinone if we heat a little of the powder of bearberry leaves.

As a test of the hydroquinone we may make use of a watery solution of quinone, with which we obtain the brown laminæ of quinhydrone. The identification by p-nitrosodimethylaniline is also here better, because it is more sensitive (Behrens). Yellowish crystal-rosettes with often leaf-like branch-ends (see diagram 9) spread out.

I take the opportunity here of expressing thanks to Mr. Grossglauser for making the diagrams.

[11] Not to be confused with the greenish crystals of the nitrosocompound.

A DIGITALIS PREPARATION FOR INTRAVENOUS INJECTION*

By Lewis G. Freeman

EVER SINCE that English herb woman of the Eighteenth Century, exercising her knowledge of herbs, used an aqueous solution of Foxglove, which subsequently was popularized by a Dr. Withering, of Birmingham, England, for its remedial quality as a heart "tonic"—a controversy, concerning the relative advisability of recognizing certain preparations of Digitalis, as having a definite therapeutic action, has ensued.

The U. S. P. still includes this infusion as one of the two digitalis preparations recognized—the other being the tincture, an alcoholic extraction using 10 per cent. drug with a 4 + 1 alcohol (95 per cent.). The International Protocol gives this tincture the title Digitalis tinctura P. I., making it a world standard.

The latest edition of the Dutch *Pharmacopœia,* the standard of the Netherlands, also has an aqueous extraction of digitalis but differing from the U. S. P. product in procedure. At the suggestion of E. Fullerton Cook, chairman of the Revision Committee of the U. S. P., a series of samples were made to determine the relative value of the methods.

The translation of the text as given in the Dutch *Pharmacopœia* is:

Digisol for Injection

Macerate one part of powdered digitalis leaf (No. 30) with eight parts of water, with frequent shaking during forty-eight hours at a temperature not exceeding 15 degrees C. Strain, let settle, pour off the clear portion of the solution, as far as possible, and filter the rest.

Shake the combined clear extract, frequently and vigorously, during forty-eight hours, with an equal amount of chloroform in an almost completely filled flask so that the formation of an emulsion is prevented as much as possible.

Collect the chloroform layer and evaporate the watery liquid, after measuring its volume, on a steam bath to a thick extract. Mix this extract with sufficient dried sodium sulphate, so that, after thorough

*A thesis presented to the Philadelphia College of Pharmacy and Science in partial fulfilment of the requirements for the degree of Bachelor of Science in Pharmacy.

rubbing, a uniform powder is obtained. Shake this mixture frequently and vigorously during twenty-four hours, with as much of the chloroform extract as corresponds to the watery solution evaporated. Filter, measure the volume of chloroform and distill it off. Stir the residue from the chloroform extraction frequently and vigorously, with as much water, added in successive amounts, as the volume of the chloroform used.

Dissolve in the solution 0.8 per cent. of sterile sodium chloride, filter, adjust for activity, and sterilize (pasteurize) in suitable containers on three successive days for one hour at a temperature of 70 to 80 degrees C.

Clear, almost colorless, very slightly green liquid, smelling distinctly of digitalis leaf, the taste being very bitter and the liquid foaming upon shaking.

The fatal dose, measured as described under digitalis leaves, must be 2 cc. of digitalis solution (digisol for injection) per kg. of cat.

If 1 cc. of the digitalis liquid is evaporated and the remainder is dissolved in 1 cc. strong acetic acid, to which is added a trace of ferric chloride, all being superimposed upon sulphuric acid, the border zone must be red-violet and the layer above blue-green.

It must be kept sterile, away from light and in a cool place.

In addition to this intravenous preparation, one for oral administration is recognized following the same procedure for extracting the active principles with the exception that in place of Sterile Sodium Chloride 0.85 per cent. prior to pasteurization ethyl alcohol (95 per cent.) equivalent to 10 per cent. of the finished product is added as preservative.

The similarity of the titles of these two preparations DIGISOL—and the American—DIGITOL—should not lead to confusion, for in physical appearance they are different. Digisol—Dutch—a clear yellow amber yellow solution; Digitol—American—a dark green solution with a strong alcoholic odor similar to the U. S. P. tincture.

Four samples were made using leaves personally selected and collected during the preflowering state of September, 1927, and divided according to size and part of the plant selected. They were assorted into three lots known as: 1. Large leaves. 2. Small leaves. 3. Leaves from the entire stalk. These were dried as recommended in the Dutch *Pharmacopœia* under Digitalis leaf, at a temperature of 55-60 C. and comminuted to a No. 30 powder. These are samples B, C, D, F.

Two samples were prepared from leaves such as used by American manufacturers of Digitalis preparations, which were sun-dried and only coarsely comminuted. These are samples A, E.

Table A gives the quantities used and obtained through various stages of development of each sample and the lot of drug used for each.

Sample	*Lot Leaf*	*Drug Gm.*	*Water Ext. Cold Water Maceration cc.*	*Water Ext. after Expression cc.*	*Water-Ext. after Filtration cc.*	*$CHCl_3$ after Ext-ion cc.*	*$CHCl_3$ B:P: C.*
A	Com.	500	4000	3310	3200	3165	61-67
B	Lg.	500	4000	3150	2370	2310	61-69
					605	575	61-69
C	Sml.	250	2000	1560	1500	1400-a	61-68
D	W:P:	250	2000	1600	1570-b	1519	61-69
E	Com.	250	2000	1550	1500	1456	61-69
F	Lg.	250	2000	1570	1445	1385	61-69

a—centrifuge only.
b—incomplete filtration.

The volume yields of the first water extract at 15 degrees C. were materially increased (approximately 10 per cent.) by using a drug press so that a greater amount of the water soluble principles would be obtained. This was equivalent to about 80 per cent. of the volume of water originally used for maceration.

The above expression from the drug press required filtration. To do this most efficiently (clarity and time factor) it was necessary to use suction filtration. This reduced the volume for chloroform extraction.

In the extraction with an equal volume of chloroform, the importance of having the container completely filled was very essential. The saponin formed an emulsion with the chloroform. There was great difficulty in breaking this emulsion. Centrifuging was attempted. By using exsiccated sodium sulphate, and shaking with the emulsion, separation was increased but in none of the samples was the last cc. separated. This residue was a thick, slimy, grayish-brown mixture.

The concentration of the aqueous extract after chloroform extraction, to the pilular consistence, was done in a vacuum drier at 35-37 degrees C. in order to insure a uniform product from the large volume of aqueous solution. Water bath treatment was tried with a

portion of sample A but as this solution approached pilular consistency, carbonization was indicated around the outer edge of the dish.

The chloroform extraction after the maceration with the pilular extract, that was reduced to powder form with exsiccated sodium sulphate, was filtered and the chloroform distilled off on a water bath. Approximately the first 50 per cent. came over at 61 degrees C. The temperature rose to 64 degrees C. for the next 25 per cent. and then to 67 degrees C. until only about 5 per cent. remained when it was necessary to use 69 degrees C. and this distilled over very slowly.

The thick concentrated syrup, of amber greenish-black color, was poured into a tared beaker and the residue in the flask rinsed into this beaker using five to eight portions of ½ cc. of distilled $CHCl_3$. This was evaporated at 20 degrees C. until a non-fluid mass resulted. Further drying to a constant weight was effected by keeping in a fresh calcium chloride desiccator. The yield of total solids thus extracted was equivalent to 1 to 2 mg. per gm. of drug used at the beginning.

There was considerable variation in the solubility of this extract. In none of the samples was the entire residue soluble, based upon the color, odor and taste obtained, by adding water in successive portions, as directed in the Dutch *Pharmacopœia*. In order to make solution as complete as possible several methods were tried.

Sample A + B. The chloroform extract was thoroughly treated with successive volumes of water (25 to 50 cc.) and a clear, yellow solution resulted having the peculiar penetrating odor of Digitalis and an intensely bitter taste. After a practically colorless, odorless and tasteless solution resulted, there still remained a gummy, yellow-gray residue. Each of the combined water solutions were allowed to macerate with their respective residues in an icebox for two months. An insoluble portion was still evident. In sample A after filtering clear, the residue which was dissolved in a volume of alcohol (95 per cent.) equal to 1/10 of the water, making it equivalent in alcohol content to the oral preparation of the D. P. This alcoholic solution A-1 produced a more intense yellow color as compared to sample B.—aqueous.

Sample C. Trituration of the dried $CHCl_3$ extract with successive portions of water (10-20 cc.) was limited to ten-minute periods continuing until the final portion was colorless and almost tasteless. The residue was further extracted with a volume of alcohol (95 per cent.) equal to 1/10 of the water and then more water was added. This solution was called C-1 and kept for separate biologic standardization.

Samples D, E, F. A total volume of 100 cc. of water were used for each sample in the triturations. The addition of alcohol to the insoluble residue was again used. In sample D, when decantation of the aqueous expression of the last 25 per cent. by volume had not responded to suction filtration; this insoluble gummy residue, on addition of the alcohol, produced a pale green turbid solution as compared to samples E and F which were clear yellow solutions.

Instead of using the cat method of standardization, the guinea pig and U. S. P. frog method were tried. Through the courtesy of Professor E. Fullerton Cook samples of both the oral and intravenous preparations were obtained and the M. L. D. of these were determined. Dr. Thomas S. Githens rendered valuable assistance in the work with both methods. The following table B represents the guinea pig determinations:

Sample	*cc. per Gm.*	*Doses per Gm. Mngn.*	*Doses per 250*	*Wt. Gm.*	*Dose cc.*	*Live*	*Died*
D. P. Int.	....	....	2.5	300	3.	*	
D. P. Oral	....	....	5.	290	5.8	*	
A	1.0	2.0	0.5	320	0.64	*	
A	1.0	1.3	0.75	310	0.93		*
A-1	0.1	0.13	0.75	300	0.9	*	
B	3.0	3.0	1.	350	1.4	*	
B	3.0	2.5	1.25	335	1.7		*
C	0.4	1.0	0.4	330	0.53	*	
C	0.4	.5	0.75	300	0.9		*
C-1	0.16	1.	0.16	300	0.2	S.	
C-1	0.16	.8	0.20	300	0.24		*
D	0.4	1.3	0.3	320	0.38	*	
D	0.4	1.0	0.4	340	0.54		*
D-1	0.2	2.0	0.1	400	0.16	*	
D-1	0.2	1.0	0.2	290	0.23		*
D-2 Res.	2.	2.	1.0	290	1.16	*	
D-2 "	2.	1.	2.	290	2.3		*
E	0.4	1.2	0.75	310	0.93	*	
E-100	0.2	1.0	0.2	290	0.23	*	
E-1	0.2	0.5	0.4	325	0.52		*
F	0.4	1.0	0.4	375	0.60	*	
F	0.4	0.5	0.8	275	0.88		*
F-1	0.2	2.0	0.1	360	0.144	*	
F-1	0.2	1.0	0.2	280	0.225		*
F-2	1.0	1.0	1.0	285	1.14		S-D 48 hr.
F-2	1.0	0.4	2.5	370	3.70		*

From the above, the M. L. D. of the European product shows a low potency. A shortage of animals prevented obtaining an M. L. D. but the indications were that more 2.5 doses per gram were necessary for the intravenous solution and greater than 5.0 doses per gram in case of the oral.

Furthermore, it was evident that the corresponding value of my samples in both aqueous and 10 per cent. alcoholic solutions was lower and having a known M. L. D., and that even though alcohol was added for further extraction in Sample A, no M. L. D. representing a degree of potency was indicated. In Samples C, D, and F, where solution of the active principle was done in an hour or two, then further extracted using alcohol, these two samples showed M. L. D. that were practically equivalent. The aqueous extraction E was low but the alcoholic solution was correspondingly higher.

Samples D-2 and F-2 represent definite dilutions of the residue left after filtering the chloroform extracts prior to distillation. Apparently some active principle, chloroform insoluble but water soluble, was present because an M. L. D. was found.

The following table C represents the U. S. P. frog figures 1 hour at 20 degrees C.:

	Frog Gm.	*cc. per Gm. Mngn.*	*Oubain cc. used*	*1-10,000 Result*
	22	.0045	0.098	Beat
	23	.0050	0.115	Syst.
	36	.0050	0.180	"
	34	.0055	0.187	Dead
		AQUEOUS DIGITALIS SAMPLES		
Europ. Int.	32	.015	.480	Beat
" "	38	.0225	.750	"
	30			
" Oral	40	.015	.600	Beat
	28	.020	.560	"
	24	.025	.600	"
	30	.030	.900	"
A	46	.010	.460	Dead
	44	.008	.342	"
	21	.007	.147	Syst.
	41	.006	.246	Beat
B	24	.015	.360	Dead
	30	.012	.360	Syst.

	Frog Gm.	*cc. per Gm. Mngn.*	*Oubain cc. used*	*1-10,000 Result*
	38	.010	.380	Beat.
	30	.009	.270	"
C	34	.015	.510	Dead
	36	.010	.360	"
	26	.008	.208	"
	30	.007	.210	Syst.
D	32	.015	.480	Dead
	34	0.10	.340	"
	22	.008	.176	Syst.
	30	.007	.210	Beat
E	30	.015	.450	Dead
	36	.010	.360	"
	28	.008	.224	Syst.
F	30	.015	.450	Dead
	36	.010	.360	"
	26	.008	.208	Syst.
		ALCOHOLIC EXTRACTIONS		
C	22	.015	.330	Dead
D	24	.015	.360	"
	20	.0075	.150	"
E	30	.015	.450	"
F	24	.015	.360	"
	42	.0075	.315	"

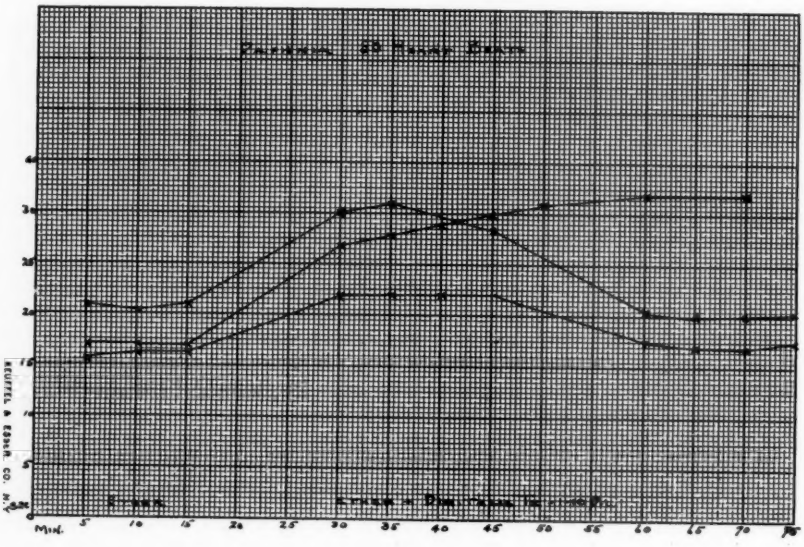
It is thus evident that the European had a much lower degree of potency compared to a normal tincture and that my aqueous samples showed a higher M. L. D.—that sample B which more nearly represented the dilutions in a volume of water equal to the volume $CHCl_3$, recommended in D. P., was more than three times as potent as the European samples—that the five other samples possess a still higher degree of potency and that the alcoholic solutions have a correspondingly high degree of activity. Limited time prevented an M. L. D. of these solutions.

In conjunction with the determination of the foregoing biologic standards, at the suggestion of Dr. Arno Viehoever, the possibility of using Daphnia, a water flea, as a practical means for evaluating the action of Digitalis preparations, was tried.

As the data available for this type of work is limited to records of heart beat of the etherized organisms observed microscopically, the procedure evolved is as follows:

Add 5 cc. Ether U. S. P. to sufficient distilled water to make 100 cc. solution. Use .1-.2 cc. for etherizing daphnia.

The animals are transferred from aquariums to small watch crystals using a pipette that is slowly lowered to the bottom of the container. Ordinarily capillary attraction of the water particles within the pipette to a level corresponding to the height outside draws one or more organisms with it. By means of a moist camel hair brush quickly transfer one organism from the crystal to a hanging



drop slide containing .1 cc. 5 per cent. ether solution. Observation of the organisms done with low power magnification. Etherization is essential due to normal mobility of daphnia preventing accurate observations for timing heart pulsations. In the etherized condition the organism lies upon its side and the heart is readily recognized In the event excess ether is used an irregular contraction is seen—the normal heart beat being uniform and rhythmic. Should this irregularity persist over fifteen minutes, discard the organism for further work. A split chronometer enables one to get more accurate results. The entire organism should be visible in the field under low power magnification and if less than one-half the field area should

not be used. The daphnia must be in an aqueous medium through entire observations.

The following figures were obtained employing the procedure described above, at temperature within a range of 17 degrees to 27 degrees C. More than twenty-five organisms were examined containing fifty contractions and noting elapsed time using a split second (1/5) chronometer. This was never less than fifteen seconds, nor more than twenty-one seconds. The majority were between seventeen to nineteen seconds per 50 beat. Five organisms were observed at intervals over two-hour periods—allowing organisms to come out of the ether and then etherizing (with .1 cc.), no variation was evident in rechecking heart beat. From these figures the number of beats per minute was equivalent to 150 to 200 with the average of 165 to 175 for majority.

For determination of the action of digitalis upon the organism, a series of observations using the U. S. P. tincture diluted 1 to 10. One cc. of this solution was added to the 1 cc. ether solution containing the previously observed daphnia and its heart beat. Slight acceleration was evident at first but within ten minutes a slower and stronger beat resulted—reducing the average to 100-120 beats per minute. This gradually returned to normal beat after thirty minutes' time elapsed.

Greater consistency of this change in heart beat was obtained by allowing the organism to swim about, for five- and ten-minute periods, in 1 cc. of the diluted tincture, the normal heart beat of the etherized organism having previously been determined. Its activity was visibly reduced but re-etherizing was necessary—no lethal effect evident. Normal heart beats of fifty in seventeen to twenty-one seconds were reduced to twenty-six seconds and continued at that rate for over one-half hour. (Mm. equivalent.)

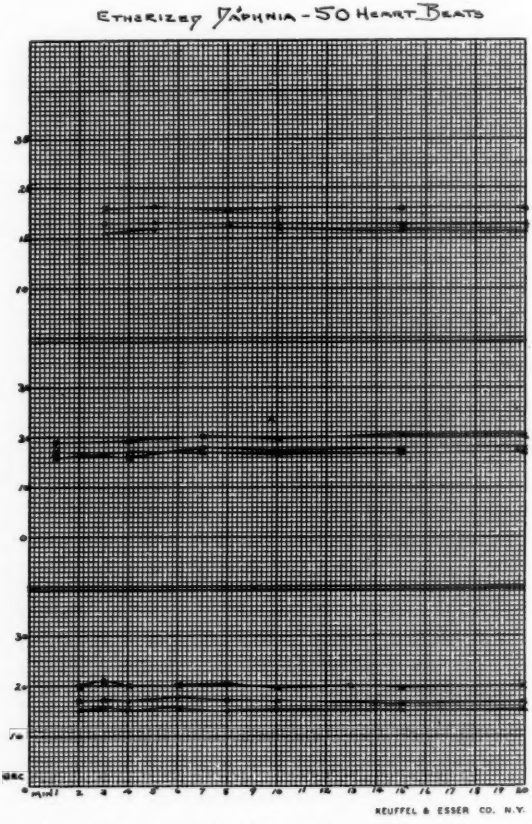
From the limited observations made using the Digisol preparations upon daphnia, toxicity was noted in two cases and on all others reduction of the heart beat again evident. Due to limited time, data was insufficient for establishing a quantitative method.

The justification for using daphnia as a quantitative test object was indicated.

The pH value of the European preparations and our samples were studied and the following results recorded:

With electrolytic determinations using calomel cathode, the European intravenous was equal to a pH of 3.5 and four months later

colorimetric determinations showed a pH value of 3.1. The pH value of the oral, by electrolytic method, was 3.6, and at the later period by colorimetric methods it was 3.2. A sample of U. S. P. tincture by colorimetric methods had a pH value of 5.7.



The colorimetric method of samples A to F gave the following pH values:

Sample	*pH.*	*Sample*	*pH.*
A	3.8	A-1	4.0-4.1
B	4.2		
C	4.1	C-1	3.8
D	3.9	D-1	3.8
E	4.1	E-1	4.1
F	3.9	F-1	4.1

These values indicate greater acidity than the U. S. P. tincture which is within the range as given by work previously done by R. B. Smith (*Journal of the American Pharmaceutical Association,* March, 1928).

Conclusions

That the imported European preparations made by this method based upon the biologic tests had a low toxicity by comparison with my samples.

That the procedure requires great care in its numerous steps—regardless of the time factor which necessitates longer periods than commonly employed for our U. S. P. preparations.

That more extensive work be done on the entire process to determine whether the active principles can be brought into solution more effectively.

That modifications in chloroform extraction might produce more effective yield of total solids.

That there is a similarity between this method and the work of Kraff on the water and chloroform soluble glucosides—but more extensive work be done to determine the nature of the chemical constituents.

That biologic standardizations indicated a difference of solubility and that alcohol further extracts soluble active principles.

That the product be standardized not only before pasteurization but also after this sterilization.

That the samples are extremely acid and based upon the European preparations this increases on ageing.

That work with daphnia be extended with the idea of establishing a new biologic method for the action of digitalis preparations.

Thanks and Appreciation

To Dr. Thomas S. Githens for his valuable suggestions and assistance throughout the entire work. To E. Fullerton Cook for European preparations. To Dr. Arno Viehoever, in conjunction with the Daphnia work. To the H. K. Mulford Company for the use of the special apparatus necessary.

ABSTRACTED AND REPRINTED ARTICLES

SODIUM ALUM*

By Henry Leffmann and Lester W. Strock

THE WORD ALUM is derived from the Latin "alumen," but the significance that the word had to the Romans has little bearing upon the significance of the English word today. The Romans understood by it certain astringent substances, mostly natural products, of about the same nature as the Greeks designated by the term "stypteria," in both cases probably aluminum or ferric compounds or mixtures thereof. As a definite English word, "alum" is found as early as 1325, but, of course, without the technical significance it now has. Within very recent time, owing to certain commercial issues, much discussion has taken place as to the exact technical scope of the term, many American experts have been brought into the dispute and much printer's ink expended on it. The gist of the dispute is the attempt of certain parties that use sodium alum, to have it excluded from the group and designated only by a term indicating the detailed chemical composition (aluminum sodium sulphate) or by a convenient mask SAS, a method now quite frequent in trade.

The literature relating to sodium alum covers more than a century, and so far as exact and careful investigation goes, there is no reason to doubt that it belongs to the same group as potassium and ammonium alum. There is no justification for relegating it to an outside position. The greater difficulty of crystallizing it has been the bar to its early introduction in place of potassium alum, since it would be cheaper, the dominating motive in trade. Ammonium alum took the place of potassium alum about the time of the War between the States, when the obtaining of ammonium compounds from gas liquor made ammonium sulphate cheaper than potassium sulphate. The substitution was made without general notice and for some time people were using ammonium alum believing that it was the alum of their fathers. The principal point is that in all cases alum is used for the aluminum salt, the other salt is merely added to secure easily a well-crystallized form, aluminum sulphate alone being somewhat un-

*Reprinted from *Bulletin, Wagner Free Institute of Science*, 1928.

satisfactory. A proof of this statement is to be found in the course followed by United States Pharmacopeia, in which "alum" has always been an item. The first edition and the first three revisions listed potassium aluminum sulphate alone, designating no other similar salt. In 1860, the commercial production of ammonium aluminum sulphate led to its recognition under its systematic name, not as alum. In 1870, however, it became the official compound brought about by the fact that it was the bulk of the alum on the market. Potassium aluminum sulphate was relegated to a side status, under its systematic name. In 1880, 1890 and 1900 potassium alum came back to official recognition, ammonium alum going into the second place. In 1910 and 1920 the framers of the work threw up their hands and admitted both forms to the designation of "Alumen, U. S. P." Now, what is the "greatest common denominator" of this series of changes? Obviously, the aluminum sulphate. As long as it is part of the compound the substance is alum. Why should sodium alum stand like the Peri at the gate, disconsolately waiting for admission to fellowship? That the essential feature of an alum is the sulphate of the trivalent element (Al, Fe, Cr, for instance) is shown by the conventional naming of the several forms. Ferric alum contains ferric sulphate, chromic alum, contains chromic sulphate. It is a universal agreement among chemists and pharmacists that if the trivalent element is not indicated, it is aluminum. Berzelius expressed the logic of the question when he said that alum is the generic title and each form is specific. (Quoted in Turner's "Elements of Chemistry," 7th edition, Philadelphia, 1846.)

As a matter of fact, sodium aluminum sulphate has been designated as sodium alum for more than a hundred years, originally by those who first obtained it in the early part of the nineteenth century. The record lies open that all who run may read. A. F. Gehlen wrote shortly before his death (1815) to Jos. N. Fuchs that he had obtained the compound in the same form as the other alums. Fuchs makes this statement in a paper in *Jour. f. Chem. u. Phys.*, 1815, *15*, 377. (This publication is often termed Schweigger's Journal.) A year later Zellner took up the matter of the production and properties of the compound, publishing his work in the same journal (1816, *18*, 344), the title being "Uber die dreifachen Verbindungen der krystallisirten schwefelsauren Thonerde." He states that he prepared sodium alum in August, 1815, but hesitated to publish the fact as he thought it might not be new. As noted above these early investi-

gators found the great difficulty to be the crystallization. Heated above 40° C. it generally fails to give definite forms. By spontaneous evaporation at room temperatures characteristic crystals are obtainable. These statements have all been confirmed in our own work. Excellent and characteristic crystals have been obtained, showing that the molecular association of the two sulphates and the water of crystallization coincides with those in the familiar alums. No doubt can be entertained that if sodium alum was as easily crystallizable as the other alums it would have long since displaced them, on account of cheapness, but labor cost is such an important item in manufactures that it has not found general use. Its imperfectly crystallized form, however, is now a familiar article and has been seized upon as a means of introducing aluminum sulphate into food. The sulphate of the monovalent element serves only the purpose of securing a satisfactory form in which to present the sulphate of trivalent element. This is true of all the alums now in commerce. Ferric alum is used as a means of employing a ferric salt in permanent and definite form, chrome alum for a similar reason.

Later studies confirm the positions here taken. James Locke in *American Chemical Journal* (1901, *26,* 166) on "Gradations in the Properties of the Alums," asserts that all compounds of the general formula $M'M'''(SO_4)_2\ 12H_2O$ in which M′ is a monovalent element and M‴ a trivalent one, are alums. He indicates nine trivalent elements that may form an alum, namely, Al, Fe, Cr, Ti, V, Ga, Co, Mn, and In. In the monovalent group, K, Na, Rb, Cs, and Tl are noted. Lithium is considered at present as not being capable of forming an alum, but lithium is markedly different in properties from the rest of the group with which it is placed in the periodic system. Ostwald said that sodium alum does not exist, a curious error in view of what has been done more than a century ago. Thallium may be expected to show some departure from the typical alum, for it has relations with several other groups. Its discoverer, Crookes, called it the *Ornithorhynchus* of metals. W. R. Smith, also in *Jour. Amer. Chem. Soc.,* 1909, *31,* 247, extended the results of earlier workers.

Zellner, as noted above, made a very comprehensive study of sodium alum. He gives the following composition:

Sulfuric acid	34.522	(expressed as anhydride)
Alumina	11.1	
Soda	6.63	(expressed as anhydride)
Water	48.010	

Each datum was determined directly and the methods are given in detail. In comparing the data with a modern analysis it must be borne in mind that the atomic weights were not exactly those now used. The Berzelian system of symbols, though published, had not come into general use.

Zellner expressed clearly and distinctly the status of the compound as follows: "Der Kürze wegen, werde ich die schwefelsaure Natrumthonerde = Natrumalaun, so wie die schwefelsaure Kalithonerde = Kalialaun, benennen." "For brevity, I will call the sodium aluminum sulphate, sodium alum, just as potassium aluminum sulphate is called potassium alum." This decisive opinion by one who may be regarded as the first to present a complete account of the compound, seems to entitle the name to positive standing. It is unfortunately true that when powerful economic interests come

Sodium alum crystals (natural size)
Prepared and photographed by the authors

into play many see, or imagine they see, distinctions and resemblances that are not appreciable to the mass of persons. Men may, and often do, find

> "* * * with keen discriminating sight
> Black's not so black, nor white so *very* white."

Hence, sodium aluminum sulphate, which for more than a century has been accepted as sodium alum, is now denied that title. It may very appropriately be asked if it is not sodium alum what is it? The answer that we may get is that it is SAS!

In our own experiments we have reviewed the work of the earliest investigators and observing the conditions they indicated have obtained results concordant with theirs. The method usually employed to secure crystals by making a solution saturated at the boiling point and allowing the liquid to cool slowly does not work well with sodium alum, possibly because of the somewhat eccentric behavior of hydrated sodium sulphate, which as is known undergoes dehydration at a tem-

perature far below 100°. Crystals have been obtained by evaporation at a moderate temperature, which have been shown by examination under polarized light to be isotropic similar to the well-known alums

Sodium alum is much more liable to effloresce than the common alums. A few minutes' exposure to free air produces a white powdery material on the edges of the crystals. As we were able to operate only on comparatively small amounts, large groups of crystals such as are commonly seen with ammonium alum were not obtainable, but perfect octahedrons of about a centimeter on the edges were produced which were clear and brilliant. The most usual form is the octahedron modified by the cube. In some experiments monoclinic crystals were obtained and also true cubes but these are not usual.

Determinations of the refractive index gave results in close agreements with the figures given in the Smithsonian Institution tables of 1920; those of Bulletin 1108 (1922), U. S. Department of Agriculture and of Groth's "Chemische Krystallographie."

Our thanks are extended to the Wagner Free Institute of Science of Philadelphia, for assistance in the work, and to the Philadelphia College of Pharmacy and Science for allowing the use of the laboratory equipment.

SCIENTIFIC AND TECHNICAL ABSTRACTS

A Simplified Method of Estimating the Silver Content of Organic Silver Preparations—An exactly weighed-out quantity of the preparation (varying according to the kind of protein and the percentage of Ag) is placed with 15 cc. HNO_3 (sp. gr. 1.20) in a titration flask on a boiling water-bath, and after half an hour mixed with 30 to 40 cc. H_2O. A few drops of $KMnO_4$ solution are then added, sufficient to retain the red color for one minute before decolorization; any excess of $KMnO_4$ can be removed with a small crystal of $FeSO_4$ ($KMnO_4$ oxidizes the N-oxides to HNO_3). The solution is then titrated in the usual way with $(NH)_4CNS$. This method requires less time than that of Lehmann, and has also the advantage that the estimation can be carried out in one flask. It was applied to Actol (0.2), Albargin (0.6), Argonin (0.8), Hegenon (0.8), Collargol (0.2), Ichthargan (0.3), Itrol (0.2), Largin (0.5), Novargan

(0.8). Protargol (0.8). (The figures in parenthesis give the quantities in gm. worked on.) The results obtained closely agree with those of other methods.—Gregor Kogan (*Pharm. Zentralhalle,* **69**, 15, 228, through *Pharm. Jour.*).

PINE OIL DISINFECTANT—An odoriferous disinfectant quite soluble in water is obtained from the following formula:

Steam-distilled Pine Oil	1000 gm.
Rosin	400 gm.
Sodium hydroxide	50 gm.
Water	150 cc.

Dissolve the sodium hydroxide in the water by means of a gentle heat. Melt the rosin in a capacious vessel and add to it the pine oil, previously heated on a water bath to about 80 degrees C. Pour the warm sodium hydroxide solution into this mixture and stir vigorously until a homogeneous product results.

ACTIVE PRINCIPLES OF THE POSTERIOR LOBE OF THE PITUITARY GLAND—A summary of an extensive record of research in connection with the foregoing subject is presented herewith. The *Journal of the American Chemical Society,* **50**, 573 (1928), published the original article, it being considered in these days more substantial to submit such manuscript to chemical societies or journals rather than to pharmaceutical societies or journals. The authors are Oliver Kamm, T. B. Aldrich, I. W. Grote, L. W. Rowe and E. P. Bugbee.

1. The posterior lobe of the pituitary gland contains two important active principles: one which raises blood pressure and another which stimulates contraction of uterine muscle.

2. A substantially complete separation of these two active principles has been accomplished by the employment of salting-out methods and, subsequently, by the use of appropriate solvents and precipitants.

3. Solutions of these separated active principles have been recombined to form a pituitary extract identical with the original from which they were prepared, thus proving that no decomposition has taken place.

4. The substantially pure pressor principle (β-hypophamine) has been obtained in the form of a white, stable, water-soluble powder 80 times as potent as the International Standard Powdered Pituitary.

5. The separated oxytocic principle (*a*-hypophamine) has been obtained in the form of a white, stable, water-soluble powder which is more than 150 times as potent as the International Standard Powdered Pituitary.

6. The pressor principle has been shown to be responsible for the diuretic-antidiuretic action of pituitary extracts.

7. The pressor principle when tested on animals for demonstration of pressor effects shows the development of tolerance which is characteristic of active pituitary extracts. It has been shown to possess no appreciable depressor action.

8. Both active principles are basic bodies, presumably amines.

9. Practical manufacturing methods have been developed for the separation of these two hormones and they have been made available to the medical profession for careful clinical trial.

10. As a result of this preliminary work the foundation is now laid for an investigation of the chemical nature of the separated hormones of the posterior lobe of the pituitary gland, together with a more exhaustive study of their pharmacological properties.

A NEW SOURCE OF BORAX—Exploitation of the kernite (also called rasorite) deposits in the Mohave Desert, Kern County, California, probably will result in killing off the mining of other borate minerals elsewhere in this country and in other countries so that the United States will have a complete monopoly, according to Dr. Waldemar T. Schaller, of the Geological Survey.

As far as is known, kernite, an entirely new mineral, exists nowhere else in the world. The deposit lies but three to four hundred feet beneath the surface, is more than 100 feet thick and extends at least 500 feet in every direction. It was discovered in 1926 and mining operations were begun approximately a year ago.

Kernite is virtually pure sodium borate. The material mined is over 75 per cent. pure mineral, the remainder being clay. To prepare it for the market it is only necessary to dissolve it in water, filter off the clay, and permit recrystallization to take place. Marketable borax is sodium borate plus ten molecules of water. Kernite is the same sodium borate plus four molecules of water. During the refining process six molecules of water are added so that one ton of kernite makes 1.4 tons or nearly a ton and a half of borax. There is probably no other commercial mineral that increases its marketable bulk in such a fashion through the process of refining.

Previous to the discovery of kernite the world's borax supply was derived principally from the minerals borax, colemanite and ulexite. Italy procured it from volcanic steam containing boric acid. In each case the process involved was complex and expensive. In this country borax was formerly secured from mineral deposits in and near Death Valley, under dangerous circumstances, and had to be hauled from the mines by the familiar "twenty-mule team," to a distant railroad.

The kernite mines are within four miles of the Santa Fe main line and a spur track, built at small expense across the intervening alluvial flat, has made transportation simple. It is estimated that enough of the mineral already has been blocked out to supply the market for some time and millions of tons for future needs require only to be shoveled out of the ground, dissolved in water, and recrystallized.

Blood Sugar in Normal Human Blood—It is customarily stated that normal human blood contains, in round numbers, 100 mg. of dextrose to each hundred cubic centimeters of blood. This is a familiar figure to most physicians—one of the physiologic "standards" from which they reckon deviations in the direction of disease. It is known that the commonly used methods for blood sugar determination yield higher values than the sugar actually present. Somogyi has devised a method for the determination of reducing nonsugars (residual reduction) and thereby for the estimation of true sugar in blood. The amount of reducing nonsugars in human blood is found to be very uniform, averaging 27 mg. per hundred cubic centimeters of blood in terms of dextrose, as determined by the Shaffer-Hartmann method. It is independent of the blood sugar level, and rises above the normal only in cases of high nitrogen retention. The distribution of reducing nonsugars in corpuscles and plasma is unequal; the average value for corpuscles is 47 mg., for plasma 10 mg. In human blood the subtraction of 27 mg. per hundred cubic centimeters from the apparent sugar, as determined with the modified Shaffer-Hartmann reagent, gives the true sugar with a maximum error of $\pm$ 4 mg. per hundred cubic centimeters. In other words, the actual circulating dextrose is notably less than the figure usually recorded in the reports of the clinical chemist.—(*Jour. A. M. A.*)

Weed-Killer Trials—A. Hill ("Scottish Journal of Agriculture," II, 203) compares the effectiveness of certain chemicals with

some proprietary weed killers. Copper sulphate applied as a fine powder at the rate of one pound per 100 square feet was the most successful treatment, a plot treated twice remaining free from weeds for three years. The best results are obtained by spreading the copper salt on a sunny day following rain, with subsequent fine weather. Heavy rain washes away the weed killer and greatly reduces its effectiveness. Disappointing results were given with iron sulphate, sulphuric acid, washing soda, common salt and carbolic acid. Proprietary weed killers gave good results with several applications, but they were less effective than copper sulphate. Sodium chlorate was the active ingredient of a non-poisonous weed killer used in one per cent. solution. It was effective if dry weather followed its application, but the paths are apt to become moss-grown afterwards. Iron sulphate is better than copper sulphate or caustic soda for eradicating moss. Green growths on damp, shaded concrete are best removed by applying caustic alkali in powder form and, after allowing this to liquefy, removing the debris with a stiff brush and then flushing with water — (Through *Pharm. Jour.*)

Assay of Paraffin Emulsions—To determine the amount of liquid paraffin present in emulsions prepared with tragacanth, E. Schulek and G. Vastagh ("Pharmazeutische Zentralhalle," May 3, 1928) recommend the following method: A mixture of 20 grams of the emulsion to be tested and 50 cc. of alcohol (96 per cent.) is heated for ten minutes on a water bath in a tared beaker of 200 cc. capacity; this heating is sufficient to cause the complete separation of the liquid paraffin. On cooling, 50 cc. of petroleum ether is added and the particles of tragacanth floating on the alcoholic layer are made to coalesce by agitation with a glass rod. The mixture is now transferred to a separator, taking care that the tragacanth remains in the beaker. The tragacanth is kneaded by means of a glass rod with four portions of 10 cc. each of petroleum ether, which are then added to the liquid in the separator. The solution of paraffin oil in petroleum ether is now filtered through cotton wool into a tared Erlenmeyer flask of 200 cc. capacity, and the alcoholic liquid extracted with three portions of 10 cc. of petroleum ether, adding the latter to the petroleum ether in the flask. The petroleum ether is now removed by distillation, the residue, consisting of liquid paraffin, is dried at 120 degrees C. and weighed. The alcoholic solution is returned to the beaker containing the tragacanth, the alcohol is evaporated, and the residue, consisting chiefly of tragacanth, is dried at 105 degrees C. to constant weight.

The authors succeeded in demonstrating the presence of saccharin in the alcoholic extract.—(Through *Pharm. Jour.*)

PLANT AND CANCER CELLS EMIT ULTRA-VIOLET RAYS—The latest sensation in scientific circles here is the discovery that the apex of certain rapidly-growing vegetable and animal tissues emit some sort of invisible radiation which has the power to stimulate the growth of living matter with which it is not in contact. When this was first announced in 1924 by Professor Alexander Gurwitch, of Moscow, it was received with considerable skepticism here, but now it has been confirmed by German investigators who are eagerly prospecting the new field of research in various directions.

Gurwitch found that if the tip of one of the rootlets of an onion or turnip was fixed so as to point at right angles to the side of another root, though as much as a quarter of an inch away, the cells in the side nearest the tip would multiply more rapidly than elsewhere and so bend the root away. That this influence was not due to the emission of some gaseous emanation from the root tip was proved by the interposition of a thin sheet between the two roots. Glass and gelatin sheets stopped the transmission of the growth stimulation power but quartz did not. This is characteristic of ultra-violet rays and Gurwitch concludes that the radiation from the root tips has a wave-length of 180-200 millimicrons, which would place it among the ultra-violet rays of high frequency.

The German botanist, N. Wagner, has repeated these experiments with bean and onion roots and measured the effect by counting under a microscope the number of new cells produced in the roots acted upon. The increase is as high as 70 per cent. in some cases. Old cells that have ceased growing show the greatest relative increase.

The German bacteriologist, M. A. Baron, has found that the radiation from onion roots will likewise accelerate the growth of anthrax bacillus and other bacteria. The growing tip of toadstools gives off these same growth-generating (mitogenetic) rays.

The Siemens Electrical Company has taken up the question and Doctors Hauser and Vahle, working in these laboratories, report that certain growing animal tissue, such as cancer, emit such rays.

These results, if confirmed, will radically revolutionize present theories of life and growth. It has hitherto been assumed that the impulse to cell subdivision was somehow due to the direct contact of certain chemical substances transmitted through the tissues, but it

now seems that an energy agency is active in vital processes, an immaterial radiation of the nature of light but of too high a frequency to be detected by our eyes.—(*Science Service.*)

BOOK REVIEWS

FIXATION OF ATMOSPHERIC NITROGEN. By Frank A. Ernst. Fixed Nitrogen Research Laboratory, U. S. Dept. of Agric. 8 vo., ix, 154 pages. Illustrated. D. Van Nostrand & Co., New York. $2.50.

This is a compact but comprehensive summary of the methods of nitrogen fixation, a procedure which has become of the greatest moment in modern industrial chemistry. While the nitrate beds of Chile are not as near exhaustion as feared some time ago, the long sea-haul to many of the greater nations makes them fearful of serious interruption of supply of important raw material in case of war. In a German work on this subject published shortly after the close of the World War, it is stated that the British blockade was so efficient that from the date of its establishment in the early months of the war until January, 1915, only 5000 tons of the nitrate entered Germany. That nation was, however, practically independent of the outside supply, having perfected the Haber process of nitrogen fixation.

Much has been done of late years by several of the great nations in establishing plants for fixing atmospheric nitrogen and in improving the procedures. The United States has been slower in this respect than some other nations, but some development has been made.

The work in hand will serve as an excellent source of information for the several methods that have been devised, topics that have to be treated somewhat historically. Both the theory and practice of the standard procedures are described in detail, and plant installations are set forth by excellent illustrations. It appears from the book that the Bucher process, from which much was expected, has not proved very satisfactory. In addition to presenting the fixation methods, the leading facts about the Chile deposits are given. The low price of the book, which is nevertheless well printed on good paper, will make it very acceptable to chemists who wish up-to-date information on the important subject of which it treats.

HENRY LEFFMANN.